Proposed Re-evaluation Decision PRVD2016-11

Clethodim

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Table of Contents

Overview 1
What Is the Proposed Re-evaluation Decision? 1
What Does Health Canada Consider When Making a Re-evaluation Decision? 1
What Is Clethodim? 2
Health Considerations 2
Risks in Residential and Other Non-Occupational Environments 3
Environmental Considerations 4
Value Considerations 5
Next Steps 6
Science Evaluation 7
1.0 Introduction 7
2.0 The Technical Grade Active Ingredient, Its Properties and Uses 7
2.1 Identity of the Technical Grade Active Ingredient 7
2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient 8
2.3 Description of Registered Clethodim Uses 8
3.0 Impact on Human Health 9
3.1 Toxicology Summary 9
3.1.1 *Pest Control Products Act* Hazard Consideration 11
3.2 Occupational and Non-Occupational Exposure and Risk Assessment 12
3.2.1 Toxicological Endpoints 12
3.2.2 Occupational Exposure and Risk Assessment 13
3.3 Dietary Exposure and Risk Assessment 14
3.3.1 Determination of Acute Reference Dose (ARfD) 15
3.3.2 Acute Dietary Exposure and Risk Assessment 16
3.3.3 Determination of Acceptable Daily Intake (ADI) 16
3.3.4 Chronic Dietary Exposure and Risk Assessment 16
3.3.5 Dietary Cancer Exposure and Risk Assessment 17
3.4 Exposure from Drinking Water 17
3.4.1 Concentrations in Drinking Water 17
3.4.2 Drinking Water Exposure and Risk Assessment 17
3.5 Aggregate Exposure and Risk Assessment 18
3.6 Cumulative Risk Assessment 18
4.0 Impact on the Environment 18
4.1 Fate and Behaviour in the Environment 18
4.2 Environmental Risk Characterization 19
4.2.1 Risks to Terrestrial Organisms 20
4.2.2 Risks to Aquatic Organisms 22
5.0 Value 23
6.0 Pest Control Product Policy Considerations 24
6.1 Toxic Substances Management Policy Considerations 24
6.2 Formulants and Contaminants of Health or Environmental Concern 24
7.0 Incident Reports 25
8.0 Organisation for Economic Co-operation and Development Status of Clethodim 25

9.0 Proposed Re-evaluation Decision 26
9.1 Proposed Regulatory Actions 26
9.1.1 Proposed Regulatory Action Related to Human Health 26
9.1.2 Proposed Regulatory Action Related to the Environment 26
10.0 Supporting Documentation 27
List of Abbreviations 29
Appendix I Clethodim Products Registered in Canada as of 29 January 2014[1] 33
Appendix II Clethodim Uses Registered in Canada as of 29 January 2014 35
Appendix III Toxicology Endpoints for Health Risk Assessments 39
Table 1 Toxicity profile of clethodim 39
Table 2 Toxicology Endpoints for Use in Health Risk Assessment for Clethodim 48
Appendix IV Agricultural Mixer/Loader/Applicator and Postapplication Risk Assessment 49
Table 1 Occupational Mixer/Loader/Applicator Exposure and Risk Assessment (Baseline PPE) 49
Table 2 Postapplication Exposure and Risk Assessment 50
Table 3 Summary of Transfer Coefficient for Clethodim 50
Appendix V Dietary Exposure and Risk Estimates for Clethodim 53
Table 1 Summary of Acute Dietary Exposure and Risk from Clethodim 53
Table 2 Summary of Chronic Dietary Exposure and Risk from Clethodim 53
Table 3 Dietary Input Characterization for Clethodim 53
Appendix VI Food Residue Chemistry Summary 61
Appendix VII Supplemental Maximum Residue Limit Information – International Situation and Trade Implications 63
Table 1 Comparison between MRLs in Canada and in Other Jurisdictions 63
Table 2 Residue Definition in Canada and Other Jurisdictions 67
Appendix VIII Environmental Risk Assessment 69
Table 1 Physical and chemical properties of clethodim 69
Table 2 Table of maximum formation of transformation products 70
Table 3 Fate and behaviour in the environment of clethodim technical grade active ingredient and its major transformation products clethodim sulfoxide, clethodim sulfone, clethodim oxazole sulfone and clethodim imine 73
Table 4 Toxicity of clethodim and transformation products to Non-Target terrestrial Species 80
Table 5 Screening level and refined risk assessment of clethodim to beneficial arthropods. 86
Table 6 Screening level risk assessment of clethodim to earthworms, bees and terrestrial vascular plants 88
Table 7 Estimated Environmental Concentrations (EEC) in vegetation and insects 88
Table 8 Further characterization of risk to Terrestrial Vascular Plants 89
Table 9 Screening level risk assessment of clethodim to birds and mammals 89
Table 10 Toxicity of clethodim and end-use products to Non-Target aquatic Species 90
Table 11 Screening level risk assessment of clethodim and transformation products for aquatic organisms 93
Table 12 Risk Quotients for aquatic organisms determined for drift of clethodim 95

Table 13 Risk Quotients for Aquatic Organisms Determined for Runoff of clethodim in Water Bodies 80 or 15 cm deep 95
Appendix IX Proposed Label Amendments for Products Containing Clethodim 97
References 103

Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the herbicide clethodim, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of products containing clethodim for sale and use in Canada.

An evaluation of available scientific information found that currently registered uses of clethodim products do not pose unacceptable risks to human health or the environment when used according to the proposed label directions. As a requirement of the continued registration for these clethodim uses, new risk-reduction measures are proposed for the end-use products registered in Canada. No additional data are being requested at this time.

This proposal affects the end-use products containing clethodim registered in Canada. Once the final re-evaluation decision is made, registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for clethodim and presents the reasons for the proposed re-evaluation decision. It also proposes new risk-reduction measures to further protect human health and the environment.

This consultation document is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of clethodim.

The PMRA will accept written comments on this proposal up to 60 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2012-02, *Re-evaluation Program Cyclical Re-evaluation*, presents the details of the cyclical re-evaluation approach.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

What Is Clethodim?

Clethodim is a selective systemic grass herbicide. It is registered for post-emergent control of grassy weeds on a variety of broadleaved crops. Clethodim products are formulated as emulsifiable concentrate or emulsion and can be applied using ground or aerial equipment. The rate of application ranges from 15.1 to 91.2 g a.i./ha, depending upon the types of crops it is used on.

Health Considerations

Can Approved Uses of Clethodim Affect Human Health?

Products containing clethodim are unlikely to affect your health when used according to proposed label directions.

Potential exposure to clethodim may occur through diet (food and water) or when handling and applying products containing clethodim. When assessing health risks, two key factors are considered: the levels where no health effects occur, and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100 times higher (and often much higher) than levels to which humans are normally exposed when pesticide-containing products are used according to label directions.

In laboratory animals, clethodim was of low to slight acute oral toxicity, and of low toxicity via the dermal and inhalation routes. Clethodim was mildly irritating to the eyes and skin, and did not cause an allergic skin reaction.

Short- and long-term (lifetime) animal toxicity tests, as well as published reviews from other regulatory agencies, were assessed for the potential of clethodim to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoint used for risk assessment was effects on the liver. There was no indication that the young were more sensitive than the adult animal. The risk assessment protects against these and any other potential effects by ensuring that the level of exposure to humans is well below the lowest dose at which these effects occurred in animal tests.

Residues in Food and Drinking Water

Dietary risks from food and water are not of concern.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects.

Acute and chronic dietary exposures to clethodim were estimated from residues of clethodim in treated crops and drinking water for different subpopulations including children and women of reproductive age. A cancer risk assessment was not required as there was no evidence of carcinogenicity.

The acute dietary exposure estimate (in other words, from food and drinking water) at the 95th percentile represents 3.6% of the acute reference dose (ARfD) for the general population and ranges from 2.4% of the ARfD (for adults 50-99) to 7.2% of the ARfD (for children 1-2 years old) for all other population subgroups when using drinking water concentrations generated from water modelling. The chronic dietary exposure estimate for the general population represents 8.7% of the acceptable daily intake (ADI) and ranges from 6.9% of the ADI (for adults 50-99) to 24.3% of the ADI (for children 1-2 years old). Thus, acute and chronic dietary risks are not of concern.

The *Food and Drugs Act* prohibits the sale of adulterated food; that is, food containing a pesticide residue that exceeds the specified maximum residue limit (MRL). Pesticide MRLs are specified for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue that does not exceed the specified MRL does not pose a health concern. Canadian MRLs are currently specified for some commodities (http://pr-rp.hc-sc.gc.ca/mrl-lrm/index-eng.php). Residues in all other agricultural commodities, including those approved for treatment in Canada but without a specific MRL, are regulated under subsection B.15.002(1) of the Food and Drug Regulations, which requires that residues not exceed 0.1 ppm. No changes are proposed to the current MRLs for clethodim. For supplemental MRL information regarding the international situation and trade implications, refer to Appendix VII of this document.

Risks in Residential and Other Non-Occupational Environments

Non-occupational risks are not of concern.

Clethodim is not registered for use in residential areas.

Occupational Risks From Handling Clethodim

Occupational risks to handlers are not of concern when used according to proposed label directions.

Risks to handlers are not of concern for all scenarios. Based on the precautions and directions for use on the original product labels reviewed for this re-evaluation, risk estimates associated with mixing, loading, and applying activities exceeded target dermal and inhalation margins of exposure (MOEs) and are not of concern.

Postapplication risks are not of concern for all uses.

Postapplication occupational risk assessments consider exposures to workers entering treated sites in agriculture. Based on the current use pattern for agricultural scenarios reviewed for this re-evaluation, postapplication risks to workers performing activities, such as scouting, exceeded target dermal MOEs and are not of concern. A standard restricted entry interval of 12 hours is proposed for agricultural sites.

Environmental Considerations

What Happens When Clethodim Is Introduced Into the Environment?

When used according to proposed label directions, products containing clethodim are not expected to pose an unacceptable risk to the environment.

When clethodim is released into the environment, it can enter soil and surface water. In soil, clethodim breaks down quickly, and therefore, it is not expected to move downward through the soil and enter groundwater. In aquatic environments, clethodim is slightly persistent. Clethodim is not expected to accumulate in the environment or in the tissues of organisms. The major breakdown products of clethodim (clethodim sulfoxide and clethodim sulfone) are slightly persistent and highly mobile in soil and are expected to reach groundwater. However, groundwater modelling based on chemical fate data and conservative assumptions indicate that clethodim sulfoxide and clethodim sulfone will not enter groundwater at levels that could pose unacceptable risks to human health or the environment.

Clethodim does not pose a significant risk to most terrestrial organisms (earthworms, bees, birds and mammals). If clethodim is used at labelled application rates without any risk reduction measures, it may cause adverse effects on plants, certain beneficial insects and aquatic organisms (freshwater invertebrates and amphibians). Therefore, mitigation measures in the form of spray buffer zones and hazard statements are required in order to reduce potential exposure of non-target organisms. When used according to proposed label directions, clethodim is not expected to pose an unacceptable risk to the environment.

Value Considerations

Clethodim contributes to weed management in many important crops grown in Canada when used in accordance with label directions.

Clethodim is a useful herbicide for Canadian producers due to its selectivity for annual and perennial grasses along with its tolerance by broadleaved crops. It is applied post emergence to weeds and crops and can be tank mixed with many other herbicides. It is one of the broadest spectrum grass herbicides available to Canadian growers and one of few grass herbicides providing effective control of perennial grassy weeds. It is widely used in a variety of important crops grown in Canada such as canola, pulses and other oilseed crops. Clethodim is registered for use on many minor use crops and is the only herbicide registered on Prairie carnation. It is the only alternative grass herbicide to sethoxydim in many minor use crops. Clethodim has also been identified as a priority by Canadian growers for many commodities.

Proposed Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human health and the environment. These directions must be followed by law. As a result of the re-evaluation of clethodim, the PMRA is proposing further risk-reduction measures in addition to those already identified on product labels. Additional proposed risk-reduction measures are discussed below.

Human Health

To protect applicators:

- Additional label statements to clarify the protective equipment for workers applying clethodim.

To protect workers entering treated sites:

- Clarification that clethodim is not registered for use in greenhouses.

To protect bystanders from spray drift:

- A statement to promote best management practices to minimize human exposure from spray drift or spray residues resulting from drift.

Environment

To protect non-target terrestrial and aquatic habitats:

- Spray buffer zones ranging from 1 to 60 meters and 1 to 10 meters to protect non-target terrestrial and aquatic habitats, respectively, from pesticide spray drift.
- Instructions on product labels for reducing run-off.

To protect groundwater:

- A statement on product labels informing users of the leaching potential of these chemicals and identifying soil and water table conditions that may result in ground water contamination (permeable soils, shallow water table).

Next Steps

Before making a final re-evaluation decision on clothianidin, the PMRA will consider all comments received from the public in response to this consultation document. A science-based approach will be applied in making a final decision on clothianidin. The PMRA will then publish a Re-evaluation Decision[2] that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

[2] "Decision statement" as required by subsection 28(1) of the *Pest Control Products Act*.

Science Evaluation

1.0 Introduction

Clethodim is a herbicide registered for post-emergent control of grassy weeds on a variety of broadleaved crops. It belongs to the cyclohexanedione chemical family and is classified as a Weed Science Society of America Group 1 herbicide. The herbicidal activity of clethodim is due to the inhibition of the initial enzyme in the synthesis of fatty acid, acetyl CoA carboxylase (ACCase), used in building new membranes required for cell growth.

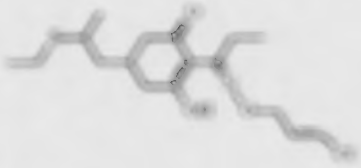
Following the re-evaluation announcement for clethodim, the registrants of the technical grade active ingredient indicated their support for continued registration of all uses included on the labels of end-use products containing clethodim in Canada. Currently registered Canadian products containing clethodim are listed in Appendix II.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name		Clethodim
Function		Herbicide
Chemical Family		Cyclohexane oxime
Chemical name		
	1 International Union of Pure and Applied Chemistry (IUPAC)	(5*RS*)-2-[(1*EZ*)-1-[(2*E*)-3-chloroallyloxyimino]propyl]-5-[(2*RS*)-2-(ethylthio)propyl]-3-hydroxycyclohex-2-en-1-one
	2 Chemical Abstracts Service (CAS)	2-[1-[[[(2*E*)-3-chloro-2-propen-1-yl]oxy]imino]propyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one
CAS Registry Number		99129-21-2
Molecular Formula		$C_{17}H_{26}ClNO_3S$

Structural Formula



Molecular Weight 359.9

Based on the manufacturing process and composition of human health or environmental concern as identified in the Canada Gazette, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including DNBP, Track 1 substances, are not expected to be present in the product.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 20°C	$< 1 \times 10^{-7}$ mPa
Ultraviolet (UV)/visible spectrum	pH λ_{max} (nm) acidic 261 neutral 283 basic 285 *No absorbance at > 300 nm*
Solubility in water at 20°C	12.0 mg/L (at pH 6.2) > 40 g/L (at pH 7) *Solubility is dependent on pH*
n-Octanol/water partition coefficient at 20°C	Log K_{ow} = 0.8; K_{ow} = 2.2×10^{0} (pH 5.35)
Dissociation constant	pK_a = 8.16

2.3 Description of Registered Clothianidin Uses

Appendix I lists all clothianidin products that are registered under the authority of the *Pest Control Products Act* as of 29 January 2016.

Appendix II lists all the Commercial Class uses for which clothianidin is currently registered. All uses were supported by the registrant at the time of initiation of re-evaluation and were, therefore, considered in the health and environmental risk assessments. Appendix II also includes the uses that were added through the PMRA's Use Requested Minor Use Label Expansion (URME) program.

Uses of clothianidin belong to the following use site categories: industrial oil seed crops and fibre crops, terrestrial food crops and terrestrial feed crops.

3.0 Impact on Human Health

3.1 Toxicology Summary

Clethodim is a selective cyclohexanedione herbicide which exerts its effect in plants by inhibiting acetyl-coenzyme A carboxylase, an essential enzyme in the fatty acid biosynthetic pathway.

A detailed review of the toxicological database for clethodim was conducted, including the more recent studies that assessed neurotoxicity and immunotoxicity. The scientific quality of the data is acceptable and the database is considered adequate to define the majority of the toxic effects that may result from exposure to clethodim.

Oral metabolism/excretion studies in the rat with radio-labelled clethodim indicated rapid absorption and excretion. Excretion of the ^{14}C-label primarily occurred in the urine with lesser amounts excreted via the feces and in exhaled breath. After 7 days, the total amount of radiolabel recovered from organs and tissues in each of the low, high and repeat dose groups was less than 1% of the administered dose. The concentration in the tissues was adrenals > liver > kidney > bone, spinal cord, followed by the remaining tissues. The major metabolite of clethodim was clethodim sulfoxide; in addition, smaller amounts of clethodim, clethodim sulfone, imine sulfoxide and 5-OH sulfone were present in the tissues. A metabolic pathway was suggested in which clethodim is rapidly oxidized to clethodim sulfoxide. Clethodim sulfoxide can be further oxidized to clethodim sulfone, deoxyalkylated to the imine sulfoxide or hydroxylated at the 5-position of the ring to yield 5-OH sulfoxide or 5-OH sulfone.

In acute toxicity testing, clethodim was of low toxicity in mice and of slight toxicity in rats by the oral route. It was of low toxicity in rabbits by the dermal route. Clethodim was of low acute toxicity by inhalation in rats, mildly irritating to the rabbit eye and skin, and a non-sensitizer in guinea pigs by a modified Buehler test.

In short- and long-term dietary studies, the primary effects were on the liver and the blood. Liver effects in short-term mouse, rat and dog studies were mostly adaptive, and included increased liver weight, and increased centrilobular hypertrophy. In the 13-week dietary rat study, increased liver weight and hypertrophy were reversed following a 6 week recovery period. Regenerative anemia was noted in short-term studies with decreases in red blood cell count, hemoglobin, and haematocrit, bone marrow hyperplasia and pigment in liver and spleen. Decreases in body weight/body weight gain and food consumption were also noted. Repeated dermal exposure in rats produced a similar toxicological profile as in oral studies (in other words, reduced body weight and liver effects) in addition to dose-related skin irritation in treated animals.

Additional treatment-related effects in repeat-dose dietary studies, either at the dose levels at which the principle effects on liver, blood and body weight first appeared, or at higher doses, were specific to one or more species. These included focal liver coagulative necrosis at higher doses in mice, focal kidney regeneration, increased serum uric acid and clinical chemistry changes at the same and higher doses in rats, and centrilobular hepatocyte vesiculation/vacuolization, bone marrow hypercellularity and clinical changes at the lowest

observed adverse effect level (LOAEL) in dogs. At higher doses, dogs also showed increased thyroid weight, chronic cystitis and focal haemorrhage in the bladder, and inflammation of the vascular trunk and degenerative cardiomyopathy in the heart; clinical chemistry findings included increased serum cholesterol, triglycerides, and alanine aminotransferase.

With chronic oral dosing, effects similar to those seen in short-term studies were observed, albeit at lower doses, suggesting a correlation between toxicity and duration of exposure. No evidence of carcinogenicity was seen in dietary studies in the mouse or rat. Overall, a battery of genotoxicity tests was negative. In mice, in addition to increased centrilobular hypertrophy and increased liver weights, there was an increased incidence and severity of amyloidosis and regenerative anaemia with decreases in red blood cell count, haemoglobin, and haematocrit. In rats, in addition to the liver effects, there were reductions in body weight and an increased incidence of chronic pancreatitis.

In a dietary two-generation reproductive toxicity test, sensitivity of the young was not apparent. Effects were limited to body weight reductions in parents and pups as well as occasional reductions of food intake in parents. Results of oral developmental toxicity studies in the rat and rabbit did not reveal sensitivity of the young. Rat fetuses showed signs of developmental delay at doses affecting body weight, uterine weight and clinical signs in the dams. At a higher dose there was an increase in external and visceral fetal malformations and an increase in maternal mortality. In rabbits, there was a slight increase in skeletal variations in fetuses at higher dose levels than the doses that were maternally toxic. Maternal toxicity included a reduction in body weight gain and decreased food consumption.

In an acute oral neurotoxicity study in rats, clinical signs of toxicity included a reduction in spontaneous activity, hunched posture, ruffled fur, abnormal gait, salivation and head tilt, and some evidence of nerve fibre degeneration in the ventral lumbar root. Effects were only evident at a dose that approached an acutely lethal level. Effects in the 13-week dietary neurotoxicity study in rats were limited to reduced body weight, body weight gain, food consumption and increased liver weight. There was an equivocal increase in minimal degeneration of the axonal sciatic nerves in high dose males, but higher incidences of minimal sciatic nerve degeneration were found equally in the control and high dose females. No treatment-related effects were noted on motor activity or in functional observation battery assessments. Overall, there is weak evidence for a neurotoxic effect.

In a 28-day dietary immunotoxicity study in mice there was equivocal evidence for an immunotoxic effect based on non-statistically significant reductions in spleen weight and antibody response. Similar effects were not observed in the range-finding study with comparable dose levels. Increased liver weight was observed in both studies.

Several toxicity studies were conducted with select plant metabolites of clethodim. In acute gavage toxicity tests, imine sulfone and 5-OH sulfone were less acutely toxic than clethodim. In 5-week dietary toxicity studies with these two metabolites, no toxic effects were noted with 5-OH sulfone, while several effects were noted at the high dose with imine sulfone (reduced body weight gain and food consumption during the first week, increased reticulocytes, cholesterol and liver weight). Supplementary developmental toxicity studies did not identify potential developmental effects for either metabolite.

Genotoxicity studies involving these metabolites, which included reverse mutation tests with strains of *Salmonella typhimurium*, and a chromosome aberration test with Chinese hamster ovary (CHO) cells, were negative with both imine sulfone and 5-OH sulfone.

3.1.1 *Pest Control Products Act* Hazard Consideration

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, as well as potential pre- and post-natal toxicity. A different factor may be deemed appropriate on the basis of reliable scientific data.

The toxicity database is currently considered complete. The database for clethodim contains a full complement of required studies including developmental toxicity studies in rats and rabbits and a reproductive toxicity study in rats. With respect to potential pre- and post-natal toxicity, none of the three studies showed sensitivity of the young. In the rat developmental toxicity study, increases in skeletal variations in the fetuses and a decrease in fetal weight, occurred at a dose at which maternal toxicity, including decreases in body weight and increased clinical signs of toxicity, also occurred. At the highest dose at which malformations occurred in the fetuses, there was severe maternal toxicity with marked clinical signs, decreased body weight and mortality, indicating an excessive dose was employed. In the rabbit developmental toxicity study, maternal effects, in the form of a slight decrease in body-weight gain, occurred at a lower dose than fetal effects. At a higher dose there was clear maternal toxicity (decreased body-weight gain, food consumption and food efficiency) and slight fetotoxicity (slight increase in skeletal variations). In the rat reproductive toxicity study, a decrease in body weight in parents and pups occurred during the latter part of lactation at the same dose level.

Overall, the database is adequate for determining the sensitivity of the young. The fetal effects observed were either minor in the presence of minor maternal toxicity, or, in the case of more severe effects, did not occur except in the presence of severe maternal toxicity. Therefore, the *Pest Control Products Act* factor was reduced to 1-fold for both acute and repeat exposure scenarios.

3.2 Occupational and Non-Occupational Exposure and Risk Assessment

Occupational and non-occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required

3.2.1 Toxicological Endpoints

3.2.1.1 Toxicology Endpoint Selection for Occupational and Non-Occupational Risk Assessment

Short- and intermediate-term dermal risk assessment

The 28-day dermal rat study with a systemic no observed adverse effect level (NOAEL) of 100 mg/kg bw/day was selected for risk assessment. At the lowest observed adverse effect level (LOAEL) of 1000 mg/kg bw/day, an increased incidence of urogenital discharge, increased liver weights, and decreased body weight were noted. For the dermal route of exposure, a target MOE of 100 was selected. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intra-species variability were applied.

Short- and intermediate-term inhalation risk assessment

The 90-day dietary rat study with a NOAEL of 25 mg/kg bw/day was selected for risk assessment. At the LOAEL of 134 mg/kg bw/day, increased incidence of centrilobular liver hypertrophy and focal regeneration of the kidney were observed. An oral study was used for inhalation risk assessments because no route-specific inhalation toxicity studies were available. For the inhalation route of exposure, a target MOE of 100 was selected. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intra-species variability have been applied.

3.2.1.2 Aggregate Risk Assessment

Clethodim is not registered for residential or non-occupational uses, therefore, the aggregate risk assessment considered exposure from food and drinking water only (please refer to Section 3.5).

3.2.1.3 Cancer Assessment

There was no evidence of carcinogenicity and therefore, no cancer risk assessment is necessary.

3.2.1.4 Dermal Absorption

A dermal absorption value was not required as a dermal endpoint was selected for the dermal route of exposure.

3.2.2 Occupational Exposure and Risk Assessment

Workers can be exposed to clethodim through mixing, loading, or applying the pesticide, and when entering a treated site to conduct activities such as scouting.

Mixer, Loader, and Applicator Exposure and Risk Assessment

There are potential exposures to mixers, loaders, and applicators. The following scenarios were assessed:

- Mixing/loading liquids;
- Groundboom application to alfalfa seedling, beans (dry), blueberry (high bush), canola, chickpea, coriander, cranberry, fenugreek, flax, lentil, mustard, onions, pea, potato, prairie carnation, safflower, soybean, spinach, sunflower;
- Aerial application to beans (dry), canola, chickpea, flax, lentil, mustard, pea, potato, soybean, sunflower;
- Mixing/loading/application by manually pressurized handwand to blueberry (high bush), cranberry;
- Mixing/loading/application by backpack to blueberry (high bush), cranberry;
- Mixing/loading/application by mechanically pressurized handwand to cranberry;

Based on the number of applications and the timing of application, workers applying clethodim would generally have a short (<30 days) duration of exposure.

Handler exposure was estimated based on the following personal protection:

Baseline PPE: Long sleeved shirt, long pants and chemical-resistant gloves (unless otherwise specified). For groundboom application, this scenario does not include gloves as the data quality was better for non-gloved scenarios than gloved scenarios.

Most dermal and inhalation exposures were estimated using data from the *Pesticide Handlers Exposure Database* (PHED), *Version 1.1*. The PHED is a compilation of generic mixer/loader applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of personal protective equipment (PPE).

Mixer/loader/applicator exposure estimates are based on the best available data at this time. Route specific MOEs for mixer/loader and applicators for agricultural crops are outlined in Appendix IV, Table 1. Calculated dermal, inhalation, and combined (total exposure from dermal and inhalation routes) MOEs for mixer/loaders and applicators of clethodim exceeded target MOEs for all uses and are not of concern.

Postapplication Worker Exposure and Risk Assessment

The postapplication occupational risk assessment considered exposures to workers who enter treated sites to conduct agronomic activities involving foliar contact (for example, scouting). Based on the clethodim use pattern, there is potential for short-term (< 30 days) postapplication exposure to clethodim residues for workers.

Activity specific transfer coefficients (TC) from the Agricultural Re-entry Task Force (ARTF) were used to estimate postapplication exposure resulting from contact with treated turf and foliage at various times after application. A TC is a factor that relates worker exposure to dislodgeable residues. TCs are specific to a given crop and activity combination (for example, hand harvesting apples, scouting late season corn) and reflect standard clothing worn by adult workers. Postapplication exposure activities include (but are not limited to): scouting, weeding, and transplanting.

Dislodgeable foliar residue (DFR) refers to the amount of residue that can be dislodged from the leaves of plants. There were no chemical-specific dislodgeable foliar residue (DFR) studies submitted to the PMRA for the re-evaluation of clethodim; therefore, the default peak value of 25% of the application rate with a dissipation rate of 10% per day was used for DFR determination.

For workers entering a treated site, restricted entry intervals (REIs) are calculated to determine the minimum length of time required before people can safely enter after application. An REI is the duration of time that must elapse before residues decline to a level where performance of a specific activity results in exposures above the target MOE.

The PMRA is concerned primarily with the potential for dermal exposure for workers performing postapplication activities in crops treated with a foliar spray. Based on the vapour pressure of clethodim, inhalation exposure is not likely to be of concern provided that the minimum 12-hour REI is followed.

Calculated dermal MOEs for worker postapplication exposure to clethodim in agricultural crops exceeded target MOEs and are not of concern. Current label REIs of 12 hours were maintained for all postapplication activities. The postapplication exposure assessment is outlined in Appendix IV, Table 2.

3.3 Dietary Exposure and Risk Assessment

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in milk and meat, may be ingested with the daily diet. Exposure to clethodim from potentially treated imports is also included in the assessment. These dietary assessments are age specific and incorporate the different eating habits of the population at various stages of life. For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food relative to their body weight when compared to adults.

Dietary risk is then determined by comparing the exposure to the dietary reference doses that are based on toxicity assessments. High toxicity may not indicate high risk if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

The PMRA considers limiting use of a pesticide when risk exceeds 100% of the reference dose. PMRA's Science Policy Note SPN2003-03, *Assessing Exposure from Pesticides – A User's Guide*, presents detailed acute and chronic risk assessments procedures.

Residue estimates used in the dietary risk assessment (DRA) may be conservatively based on the maximum residue limits (MRL) or the field trial data representing the residues that may remain on food after treatment at the maximum label rate. Surveillance data representative of the national food supply may also be used to derive a more accurate estimate of residues that may remain on food when it is purchased. These include the Canadian Food Inspection Agency's National Chemical Residue Monitoring Program and the United States Department of Agriculture Pesticide Data Program.

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model - Food Commodity Intake Database™ (DEEM-FCID™; Version 3.16) program, which incorporates food consumption data from the National Health and Nutrition Examination Survey/"What We Eat in America" (NHANES/WWEIA) dietary survey for the years 2003-2008. A cancer risk assessment was not required. For more information on dietary risk estimates or residue chemistry information used in the dietary assessment, see Appendices V, VI and VII.

3.3.1 Determination of Acute Reference Dose (ARfD)

To estimate acute dietary risk (1 day), the rat acute neurotoxicity study with a NOAEL of 100 mg/kg bw was selected for risk assessment. At the LOAEL of 1000 mg/kg bw, decreased spontaneous activity, hunched posture, ruffled fur, head tilt and abnormal gait and salivation in females were observed. These effects occurred within the first three days following a single oral dose and are therefore relevant to an acute risk assessment. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intra-species variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the *Pest Control Products Act* factor was reduced to 1-fold. Thus, the composite assessment factor (CAF) is 100.

The ARfD is calculated according to the following formula:

$$\text{ARfD} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{\text{100 mg/kg bw}}{\text{100}} = \text{1.0 mg/kg bw}$$

3.3.2 Acute Dietary Exposure and Risk Assessment

The acute dietary risk was calculated considering the highest ingestion of clethodim that would be likely on any one day, and using food consumption and food residue values. The expected intake of residues is compared to the ARfD, which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake of residues is less than the ARfD, then acute dietary exposure is not of concern.

Following the PMRA's tiered approach, basic (screening level) risk assessments were performed for all population subgroups by using MRL/tolerance-level residues for all commodities, default processing factors and assuming that all crops were 100% treated. Canadian MRLs, US tolerances or Codex MRLs, whichever was greater, were used for all crops, including imports. Drinking water contribution to the exposure was accounted for by direct incorporation of the appropriately estimated environmental concentration (EEC), obtained from water modelling (see Section 3.4 below for details), into the dietary exposure evaluation model (DEEM-FCID^{TM}).

The acute aggregate exposure estimate for clethodim at the 95th percentile for the general population is 3.6 % of the ARfD, and therefore is not of concern. The acute aggregate exposure estimates for clethodim at the 95th percentile for all population subgroups range from 2.4% to 7.2% of the ARfD, and therefore are not of concern.

3.3.3 Determination of Acceptable Daily Intake (ADI)

To estimate chronic dietary risk for the general population, the chronic toxicity/oncogenicity study in the rat was selected for risk assessment. A NOAEL of 16 mg/kg bw/day was established, with decreases in body weight gain, increases in liver weight, and an increased incidence of centrilobular hypertrophy, binucleated cells in the liver and chronic pancreatis at the LOAEL of 86 mg/kg bw/day. Standard uncertainty factors (10-fold for interspecies extrapolation and 10-fold for intraspecies variability) were applied. As previously discussed in the *Pest Control Products Act* hazard characterisation section, the *Pest Control Products Act* factor has been reduced to 1-fold. Thus, the composite assessment factor is 100.

$$\textbf{ADI} = \frac{\textbf{16 mg/kg bw/day}}{\textbf{100}} = \textbf{0.16 mg/kg bw/day}$$

The ADI provides a margin of safety of 625 to the NOAEL for fetal malformations in the rat developmental toxicity study.

3.3.4 Chronic Dietary Exposure and Risk Assessment

The chronic dietary risk was calculated by using the average consumption of different foods and the average residue values on those foods. This expected intake of residues was then compared to the ADI. When the expected intake of residues is less than the ADI, then chronic dietary exposure is not of concern.

Following the PMRA's tiered approach, basic (screening level) risk assessments were performed for the general population and all population subgroups by using MRL/tolerance-level residues for all commodities, default processing factors and assuming that all crops were 100% treated. Canadian MRLs, US tolerances or Codex MRLs, whichever was greater, were used for all crops, including imports. Drinking water contribution to the exposure was accounted for by direct incorporation of the appropriately estimated environmental concentration (EEC), obtained from water modelling (see Section 3.4 below for details), into the dietary exposure evaluation model (DEEM-FCID™).

The chronic aggregate exposure estimate for clethodim for the general population is 8.7% of the ADI, and therefore is not of concern. Exposure estimates for clethodim for population subgroups range from 6.9% to 24.3% of the ADI, and therefore are not of concern.

3.3.5 Dietary Cancer Exposure and Risk Assessment

A cancer risk assessment was not required as no cancer concerns were identified.

3.4 Exposure from Drinking Water

Residues of clethodim in potential drinking water sources were estimated from modelling.

3.4.1 Concentrations in Drinking Water

Drinking water estimated environmental concentrations (EECs) of combined residues of clethodim and its transformation products in potential drinking water sources (groundwater and surface water) were generated using computer simulation models. EECs of clethodim in groundwater were calculated using the PRZM-GW model to simulate leaching through a layered soil profile over a 50-year period. The concentrations calculated using PRZM-GW are average concentrations in the top 1m of the water table. EECs of clethodim in surface water were calculated using the PRZM/EXAMS models, which simulate pesticide runoff from a treated field into an adjacent water body, a small reservoir, and the fate of a pesticide within that water body.

A Level 1 drinking water assessment was conducted using conservative assumptions with respect to environmental fate, application rate and timing, and geographic scenario. The model was run for 50 years for all scenarios, and tested application dates between May and October. The highest ground water EEC value of 0.041 ppm for combined residues of clethodim and its transformation products was used in the acute and the chronic dietary risk assessments.

3.4.2 Drinking Water Exposure and Risk Assessment

Drinking water exposure estimates were not calculated separately. They were combined with food exposure estimates, with EEC point estimates incorporated directly in the dietary (food + drinking water) assessments. Please refer to Sections 3.3.2 and 3.3.4 for details and conclusions.

3.5 Aggregate Exposure and Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential, and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation).

As clethodim is not registered for residential or non-occupational uses, the aggregate risk assessment considered exposure from food and drinking water only. Aggregate risk from all relevant sources is not of concern. Please refer to Sections 3.3.2 and 3.3.4 for details and conclusions.

3.6 Cumulative Risk Assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. Although clethodim shares a common moiety with sethoxydim, another herbicide currently registered in Canada, the toxicology review of clethodim indicated that there is no common mechanism of toxicity between clethodim and sethoxydim. Therefore, there is no requirement for a combined assessment of clethodim and sethoxydim and/or their associated metabolites.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Clethodim is non-persistent under aerobic conditions in terrestrial systems. Biotransformation is the major route of dissipation in the terrestrial environment. Clethodim transforms into three major transformation products: clethodim sulfoxide, clethodim sulfone and clethodim oxazole sulfone, all of which exhibit similar toxicity to that of the parent. Clethodim sulfoxide and clethodim sulfone are slightly persistent, very highly mobile and are expected to reach ground and surface water. Clethodim oxazole sulfone is formed late in the breakdown process of clethodim and may persist in the environment. Based on low application rates and sequential transformation of clethodim and its major transformation products in the environment, they are not expected to accumulate and have significant carry over to the next growing season.

Clethodim, clethodim sulfoxide and clethodim sulfone are all very soluble in water. Although clethodim ranges from low to very high mobility in soil (according to criteria from McCall et. al. 1981), because it is not persistent, it is not expected to leach to groundwater and is classified as a non leacher (Gustafson, 1989). The transformation products clethodim sulfoxide and clethodim sulfone are both very highly mobile in soil and are slightly persistent, giving them the potential to leach to groundwater, according to the criteria of Cohen et al., 1984 and Gustafson, 1989.

In aerobic aquatic systems, clethodim is non-persistent to slightly persistent, while in anaerobic aquatic systems, clethodim is persistent. In water, clethodim is rapidly transformed (half-life ranges from < 3 minutes to 9.6 days) by photolysis and by microorganisms in aerobic and anaerobic aquatic systems. Major transformation products include clethodim sulfoxide, clethodim imine and clethodim imine sulfoxide. Clethodim sulfoxide and clethodim imine

sulfoxide are moderately persistent while clethodim imine is persistent and could accumulate over time. Clethodim and clethodim sulfoxide partition evenly between the water and sediment layers, while clethodim imine and clethodim imine sulfoxide are expected to partition into sediment where they may persist.

Clethodim is not expected to bioaccumulate in organisms.
The physical and chemical characteristics of clethodim are summarized in Appendix VIII, Table 1. The chemical structures and formation levels of transformation products can be found in Appendix VIII, Table 2. The environmental fate data for clethodim and its transformation products are summarized in Appendix VIII, Table 3.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats, including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (in other words, protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (*RQ*) is calculated by dividing the exposure estimate by an appropriate toxicity value (*RQ* = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods.

Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Risks to Terrestrial Organisms

A risk assessment for clethodim was conducted for terrestrial organisms. For acute toxicity studies, uncertainty factors of 1/2 and 1/10 are typically used to modify the toxicity values (EC_{25} and LC_{50}) for terrestrial invertebrates, birds and mammals when calculating risk quotients (RQs). No uncertainty factors are applied to chronic no observed effect concentration (NOEC) endpoints. A summary of terrestrial toxicity data for clethodim is presented in Appendix VIII, Table 4 and the accompanying risk assessment is presented in Appendix VIII, Table 5 for beneficial arthropods, Appendix VIII, Table 6 for terrestrial organisms other than beneficial arthropods, birds and mammals, Table 8 for further risk characterization to vascular plants and Appendix VIII, Table 9 for birds and mammals.

Invertebrates

Earthworms

Screening level risk quotients for clethodim, the transformation product clethodim sulfoxide and two end-use-products (EUPs) did not exceed the LOC on an acute basis for earthworms. The use of clethodim is not expected to pose an unacceptable risk to earthworms.

Bees

Contact exposure: Risk to bees was calculated using results from an acute toxicity test with clethodim and a separate test with a formulated EUP. The LOC was not exceeded (RQ <0.1).

Oral exposure: Toxicity endpoints from clethodim and a formulated EUP were used to determine risk from an oral exposure to bees. The LOC was not exceeded (RQ <0.1).

The use of clethodim is not expected to pose an unacceptable risk on an acute oral or contact basis to bees.

Larval bee toxicity: Exposure of bee larvae to the formulated end-use product is not expected due to rapid dissipation of clethodim at the site of application. It is considered unlikely that bees would transport end-use product material from food and pollen sources and carry it back to a hive where long term exposure could result. In addition, lack of toxicity to adult bees and lack of developmental effects on other invertebrates further confirm that clethodim would not pose unacceptable risks to larval bees.

Arthropods

Extended lab studies conducted on sprayed plants and sprayed bean leaf discs indicated that the survival and reproduction of the predatory mite, *Typhlodromus pyri*, was affected from exposure to dry residues of formulated end-use product on bean leaf discs. In similar studies, the risk quotients for the parasitic wasp, *Aphidius rhopalosiphi*, from acute and extended exposure on sprayed plants did not exceed the LOC. A refined risk assessment for *T. pyri* was conducted, looking at potential exposure from spray drift resulting from aerial and ground application.

Risks to *H. pyri* were identified, in-field and off-field, following aerial and ground applications at rates equal to and higher than the current registered lowest application rate of 67.6 g a.i./ha. The use of clothodim may pose a risk to certain foliage-dwelling arthropods and, consequently, risk reduction measures are required.

Birds and mammals

Birds

Birds showed no adverse effects to clothodim from either acute oral exposure or dietary intake. Clothodim did not affect reproduction, mortality, behaviour, food consumption or body weight of adult mallards during a 19-week exposure period. When bobwhite quails were exposed chronically through food, there appeared to be a slight treatment-related reduction (21%) in the percentage of viable embryos of egg sets at 833 mg a.i./kg diet (the highest concentration tested). The NOEL was 166 mg a.i./kg, equivalent to a daily exposure of 19.96 mg a.i./kg bw/d.

Mammals

Clothodim and the transformation product clothodim imine sulfone are practically non-toxic and slightly toxic, respectively, to mammals on an acute basis. Adverse chronic effects (reduced body weight of parent, reduced food consumption and reduced pup body weight) were seen in rats in a two generation reproduction study with clothodim.

The EEC's on food items (vegetation and insects) can be found in Table 7 of Appendix VIII.

For the bird and mammal risk assessment, the ingestion of food items contaminated by spray droplets was considered to be the main route of exposure. The risk assessment was based on the estimated daily exposure, which takes into account the expected concentration of clothodim on various food items immediately after the last application and the amount of food consumed by different sizes of birds and mammals. At the screening level, the most conservative exposure estimates are used for each animal weight category.

The screening level risk assessment indicates that acute and chronic unacceptable risks are not expected for birds and mammals exposed to clothodim (Appendix VIII, Table 8).

Terrestrial plants

Exposure of terrestrial vascular plants to clothodim end use product resulted in adverse effects on seedling emergence and vegetative vigour of monocotyledonous plants.

As multiple EC_{25} values were available for vegetative vigour, the program ETX 2.0 was used to generate a species sensitivity distribution (SSD) based on normally distributed toxicity data. The hazardous concentration to 5% of the species (HC_5) was then calculated from the SSD. The HC_5 is the concentration that is theoretically protective for 95% of species. At the HC_5 exposure level, 5% of all species will be exposed to a concentration which exceeds their LC_{50} toxicity value. The HC_5 values were used to calculate the risk quotients for terrestrial plants at the vegetative vigour stage instead of the most sensitive species tested. This provides a more scientifically robust endpoint, which uses all of the data. No uncertainty factors are applied to the HC_5 when calculating risk quotients. Using the HC_5 value from the SSD for terrestrial plants, the calculated

risk quotients exceeded the LOC at the screening level. A refined assessment looking at spray drift was conducted and indicated that non-target plants within 1m of a treated field would be exposed to clothianidin concentrations exceeding the LOC for aerial (RQ = 9.8) and for ground (RQ = 2.5) applications (Appendix VIII, Table 9). Consequently, mitigative measures, in the form of spray buffer zones, are proposed to protect non-target terrestrial plants.

6.2.2 Risks to Aquatic Organisms

A risk assessment for clothianidin was conducted for freshwater and marine aquatic organisms based on available toxicity data. A summary of aquatic toxicity data is presented in Appendix VIII, Table 10.

For acute toxicity studies, uncertainty factors of 0.2 and 0.01 are typically used to modify the toxicity values (EC_{50} or LC_{50}) for aquatic plants and invertebrates, and fish species, respectively, when calculating risk quotients (RQs). No uncertainty factors are applied to chronic NOEC endpoints. For groups where the LOC is exceeded (that is, RQ ≥ 1), a refined Tier 1 assessment is conducted to determine risk resulting from spray drift and runoff separately. Risk quotients for clothianidin and its transformation products were calculated based on the highest maximum seasonal application rate. The calculated risk quotients for clothianidin and its transformation products are summarized in Appendix VIII, Table 11 (screening level), Table 12 (Tier 1 – spray drift only) and Table 13 (Tier 1 – runoff only).

Freshwater Invertebrates

The risk quotients for freshwater invertebrates, based on toxicity studies exposing *Daphnia magna* to either clothianidin, formulated END or the transformation product clothianidin (mine or an acute basis, did not exceed the LOC at the screening level. The risk quotient for daphnids resulting from chronic exposure to clothianidin did exceed the LOC at the screening level. A refined risk assessment, looking at chronic exposure of daphnids to clothianidin spray drift, was conducted, with risk quotients exceeding the LOC for aerial application (RQ = 3.1) only. Clothianidin may pose a chronic risk to freshwater invertebrates through spray drift from aerial application and protective spray buffer zones are required.

Fish and amphibians

At the screening level, the acute exposure of freshwater fish to clothianidin, formulated END or the transformation product clothianidin sulfoxide did not exceed the LOC. A chronic risk was identified at the screening level for fathead minnow (RQ= 1.16) and amphibians (RQ= 6.1), based on the early life stage study of fathead minnow. Refined risk assessments were conducted, looking at drift and runoff. The LOC was not exceeded for the fathead minnow (RQ= 1), but was marginally exceeded for amphibians exposed to spray drift (RQ= 1.8). As the LOC was exceeded for the refined spray drift assessment, spray buffer zones are required to protect amphibians from spray drift.

Algae

Clothianidin, the formulated end use product and the transformation product clothianidin sulfoxide are not expected to pose an unacceptable risk to algae as the risk quotients did not exceed the LOC at the screening level.

Freshwater vascular plants
The risk quotient for freshwater vascular plants, based on a toxicity study with *Lemna gibba*, did not exceed the LOC at the screening level. The use of clethodim is not expected to pose an unacceptable risk to freshwater vascular plants.

Marine organisms
The LOC was not exceeded for marine invertebrates, algae and fish in a screening level risk assessment using clethodim and formulated end use product. The use of clethodim is not expected to pose an unacceptable risk to marine organisms.

5.0 Value

Clethodim is a useful herbicide for Canadian producers due to its selectivity for annual and perennial grasses along with its broadleaved crop tolerance. As a result, clethodim provides a wide application window which only needs to consider the height and growth stage of the targeted weeds because many broadleaved crops are tolerant to clethodim at all stage of growth. Clethodim can also be tank-mixed with many broadleaf herbicides to broaden the spectrum of weed control.

Clethodim is one of the broadest spectrum grass herbicides available to Canadian growers. It is one of few grass herbicides providing effective control of perennial grassy weeds. It is widely used to control grass weeds in many important crops grown in Canada such as canola, pulses and other oilseed crops. It is the only herbicide registered for use on prairie carnation. It is one of few herbicides registered for use on minor crops and often the only alternative grass herbicide to sethoxydim for use on minor crops.

Many minor uses of clethodim were registered through the User Requested Minor Use Label Expansion (URMULE) program and were identified at the time as priorities for crop production in Canada. In addition, clethodim is identified as a priority in the Canadian Grower Priority Database for a variety of crops.

Clethodim is a WSSA Group 1 mode of action herbicide (ACCase inhibitor). In Canada, populations of several key grassy weed species have developed resistance to this mode of action. Wild oats, green foxtail, large crabgrass and Persian darnel are examples of such resistant weeds reported in Canada. These ACCase inhibitor-resistant weeds affect the efficacy and broader value of clethodim. In order to prevent or delay the development of ACCase inhibitor-resistant weeds, it is crucial to maintain diversity in weed management practices.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances (those that meet all four criteria outlined in the policy, in other words, persistent in air, soil, water and/or sediment, bioaccumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*).

During the review process, clethodim and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[3] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Clethodim does not meet all Track 1 criteria, and is not considered a Track 1 substance.
- Clethodim does not form any transformation products that meet all Track 1 criteria.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[4]. The list is used as described in the PMRA Notice of Intent NOI2005-01[5] and is based on existing policies and regulations including DIR99-03 and DIR2006-02[6], and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

> Technical grade clethodim does not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*. However, clethodim end-use-products contain an aromatic petroleum distillate, and therefore, a corresponding advisory statement is proposed to be added to product labels.

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3 DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*.

4 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

5 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New* Pest Control Products Act.

6 DIR2006-02, *Formulants Policy and Implementation Guidance Document*.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

7.0 Incident Reports

Since 26 April 2007, registrants have been required by law to report incidents to the PMRA that include adverse effects to Canadian health or the environment. Information about the reporting of pesticide incidents can be found on the Pesticides and Pest Management portion of Health Canada's website. Incident reports involving the active ingredient clethodim were reviewed. As of 24 November 2014, no environmental incidents involving clethodim had been reported to the PMRA or the United States Environmental Protection Agency.

As of 17 March 2015, the PMRA had received reports of three human incidents involving clethodim. The effects in the three human incidents were considered to be at least probably associated with the reported exposure to the pest control products involved in the incidents. However, in two of the incidents, additional products were involved and as such, the role of clethodim in particular cannot be isolated. The three incidents involved dermal effects which occurred after the product splashed onto exposed skin or clothing.

These incident reports were considered in this evaluation. Overall, the findings do not impact the risk assessment as the hazard labelling already accounts for the dermal irritation properties of clethodim.

8.0 Organisation for Economic Co-operation and Development Status of Clethodim

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups member countries and provides a forum in which governments can work together to share experiences and seek solutions to common problems.

As part of the re-evaluation of an active ingredient, the PMRA takes into consideration recent developments and new information on the status of an active ingredient in other jurisdictions, including OECD member countries. In particular, decisions by an OECD member to prohibit all uses of an active ingredient for health or environmental reasons are considered for relevance to the Canadian situation.

Clethodim is currently acceptable for use in other OECD countries, including the United States, Australia and the European Union. As of 23 April 2015, no decision by an OECD member country to prohibit all uses of clethodim for health or environmental reasons has been identified.

9.0 Proposed Re-evaluation Decision

After a re-evaluation of the herbicide clethodim, Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of clethodim and associated end-use products, provided that the risk-reduction measures described in this document are implemented.

The proposed regulatory actions for clethodim are summarized in the following sections. The labels of Canadian end-use products are proposed to be amended to include the risk-reduction measures listed in Appendix IX.

9.1 Proposed Regulatory Actions

9.1.1 Proposed Regulatory Action Related to Human Health

As a result of the exposure assessment, the following clarifications are proposed to further protect human health and minimize unnecessary exposure:

- Additional label statements to clarify the protective equipment for workers applying clethodim.
- Clarification that clethodim is not registered for use in greenhouses.
- A statement to promote best management practices to minimize human exposure from spray drift or spray residues resulting from drift.

In addition, clethodim is registered for use on various crops. The residue definition (RD) in all crops and animal commodities comprises the parent clethodim and metabolites containing the 2-cyclohex-1-enone moiety. This RD is used for both enforcement and dietary risk assessment purposes. No modification to the current RDs is proposed as the result of this re-evaluation. However, it is suggested that the RD be worded as "**sum of** clethodim and its metabolites containing the 2-cyclohex-1-enone moiety, **expressed as clethodim**". The RD in drinking water for dietary risk assessment is defined as the sum of clethodim and its transformation products in water sources. See Table 2 of Appendix VII for the current and proposed Canadian RD wording, as well as the RDs of other jurisdictions.

9.1.2 Proposed Regulatory Action Related to the Environment

Clethodim, its end-use products and its major transformation products are not expected to pose an unacceptable risk to earthworms, bees, birds, small mammals, freshwater algae, aquatic plants and marine orgnisms. Clethodim may pose a risk to certain beneficial arthropods, non-target terrestrial plants, freshwater invertebrates and amphibians. In order to minimize potential exposure to clethodim in terrestrial and aquatic habitats, precautionary statements and spray buffer zones (Appendix IX) are proposed.

10.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2012-02, *Re-evaluation Program Cyclical Re-evaluation*, and DACO tables can be found on the Pesticides and Pest Management portion of Health Canada's website. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra.infoserv@hc-sc.gc.ca

The federal TSMP is available through Environment Canada's website.

List of Abbreviations

µg	microgram
ADI	acceptable daily intake
AFC	antibody forming cell
a.i.	active ingredient
ALP	alkaline phosphatase
ARfD	acute reference dose
BAF	bioaccumulation factor
BCF	bioconcentration factor
bw	body weight
bwg	body weight gain
Bz	benzyl ring label
CAF	composite assessment factor
CAS	chemical abstracts service
CFIA	Canadian Food Inspection Agency
cm	centimetres
cm^2/h	centimetres squared per hour
CMC	carboxymethylcellulose
D	day
DACO	data code
DER	data evaluation record
DFR	dislodgeable foliar residue
DHR	^{3}H-dihydrorotenone
DT_{50}	dissipation time 50% (the time required to observe a 50% decline in concentration)
EC_{50}	effective concentration on 50% of the population
EDE	estimated daily exposure
EEC	estimated environmental concentration
EFSA	European Food Safety Authority
et al.	and others
EUP	end-use products
F_1	first filial generation
F_2	second filial generation
fc	Food consumption
FIR	food ingestion rate
g	gram
GAP	Good Agricultural Practice
GD	gestation day
ha	hectare(s)
HAFT	highest average field trial
Hct	hematocrit
Hgb	hemoglobin
IRAC	Insecticide Resistance Action Committee
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_d	soil-water partition coefficient

K_F	Freundlich adsorption coefficient
K_{oc}	organic-carbon partition coefficient
K_{ow}	octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOEC	lowest observed effect concentration
LOQ	limit of quantitation
LPM	litres per minute
LR_{50}	lethal rate 50%
MAS	maximum average score
mg	milligram
MIS	mean irritation score
mL	millilitre
MOE	margin of exposure
mPa	millipascal
MP HG	mechanically pressurized hand-held sprayer
MP HW	manually pressurized hand-held sprayer
MRL	maximum residue limit
MTDB	maximum theoretical dietary burden
N/A	not applicable
NOAEL	no observed adverse effect level
NOAEC	no observed adverse effect concentration
NOEC	no observed effect concentration
NOEL	no observed effect level
OECD	Organisation for Economic Co-operation and Development
P	parental generation
PCP	pest control product
PD	Parkinson's disease
PHED	Pesticide Handlers Exposure Database
PHI	pre-harvest Interval
PMRA	Pest Management Regulatory Agency
PND	postnatal day
PPE	personal protective equipment
ppm	parts per million
PVA	polyvinyl alcohol
Pz	pyridazinone ring label
RBC	red blood cells
REI	restricted entry interval
RLD	repeat low dose
RQ	risk quotient
SHD	single high dose
SLD	single low dose
SNpc	substantia nigra pars compacta
TC	transfer coefficient

TGAI	technical grade active ingredient
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
URMULE	User Requested Minor Use Label Expansion
USC	use site category
USEPA	United States Environmental Protection Agency
UV	ultraviolet
WSP	wettable powder in water soluble packaging
♂	males
♀	females
↑	increased
↓	decreased
%CT	percent crop treated

Appendix I Clethodim Products Registered in Canada as of 29 January 2014[1]

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
22625	Commercial	Arysta Lifescience North America, LLC	Select Emulsifiable Concentrate Post-Emergence Herbicide	Emulsifiable Concentrate Or Emulsion	240 g ai/L
26426	Commercial	Bayer Cropscience Inc.	Compas Grass Herbicide	Emulsifiable Concentrate Or Emulsion	240 g ai/L
27598	Commercial	Bayer Cropscience Inc.	Centurion Emulsifiable Concentrate Post-Emergence Herbicide	Emulsifiable Concentrate Or Emulsion	240 g ai/L
28224	Commercial	Makhteshim Agan of North America Inc.	Arrow 240 EC	Emulsifiable Concentrate Or Emulsion	240 g ai/L
29277	Commercial	Loveland Products Canada Inc.	Shadow RTM Emulsifiable Concentrate Post-Emergence Herbicide	Emulsifiable Concentrate Or Emulsion	240 g ai/L
22624	Manufacturing Concentrate	Arysta Lifescience North America, LLC	Clethodim 37% Manufacturing Use Product	Solution	37%
28226	Manufacturing Concentrate	Makhteshim Agan Of North America Inc	Clethodim 37% MUP	Solution	37%
28698	Manufacturing Concentrate	Makhteshim Agan Of North America Inc	Arrow Manufacturing Use Product	Emulsifiable Concentrate Or Emulsion	240 g ai/L

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
22623	Technical Grade Active Ingredient	Arysta LifeScience North America, LLC	Clothianidin Technical	Liquid	95%
29211	Technical Grade Active Ingredient	Makhteshim Agan of North America Inc	Clothianidin Technical Herbicide	Solution	93.3%

[1] excluding discontinued products or products with a submission for discontinuation

Appendix II Clethodim Uses Registered in Canada as of 29 January 2014.

USCo[1]	Site(s)[2]	Weeds	Application Method and Equipment	Maximum Application Rate (g a.i./ha)		Maximum Number of Application Per Year
				Single[3]	Cumulative Per Year[3]	
7 13 14	Canola	Grass weeds including foxtail (green, yellow), Persian darnel, wild oats, volunteer cereals (wheat, barley, oats), barnyard grass, witchgrass, fall panicum, proso millet, volunteer corn, volunteer canary grass, quackgrass	Ground and aerial	91.2	91.2	Typically only one application is made per season. However, 2 applications at 45 g a.i./ha at a minimum 14-day interval may be used
	Canola, encollagear tolerant	Tank mix with Pursuit for control of certain broadleaf and grassy weeds	Ground	45.6	45.6	1
	Canola, glufosinate tolerant Geographic area restrictions as specified in the Application Equipment column	Tank mix with Liberty 150 SN for control of certain broadleaf and grassy weeds	Ground and aerial Prairie provinces and Peace River region of BC only	15.12	15.12	1
			Ground Eastern Canada and BC only			
	Flax (including low linolenic acid varieties)	Grass weeds including foxtail (green, yellow), Persian darnel, wild oats, volunteer cereals (wheat, barley, oats), barnyard grass, witchgrass, fall panicum, proso millet, volunteer corn, volunteer canary grass, quackgrass	Ground and aerial	91.2	91.2	Typically only one application is made per season. However, 2 applications at 45 g a.i./ha at a minimum 14-day interval may be used
	Mustard, yellow			91.2	91.2	
	Mustard, oriental (brown) - oilseed types			91.2	91.2	
13 14	Mustard, oriental (brown) - condiment					

USCs[1]	Site(s)[2]	Weeds	Application Method and Equipment	Maximum Application Rate (g ai/ha)		Maximum Number of Application Per Year
				Single[3]	Cumulative Per Year[3]	
	Lentils			91.2	91.2	
	Potatoes			91.2	91.2	
7 13 14	Soybeans			91.2	91.2	
	Soybeans, glyphosate tolerant	Volunteer glyphosate tolerant corn and other weeds	Ground	45.6	45.6	
13 14	Peas, field	Grass weeds including foxtail (green, yellow), Persian darnel, wild oats, volunteer cereals (wheat, barley, oats), barnyard grass, witchgrass, fall panicum, proso millet, volunteer corn, volunteer canary grass, quackgrass	Ground and aerial	91.2	91.2	Typically only one application is made per season. However, 2 applications at 45 g a.i./ha at a minimum 14-day interval may be used
7 13 14	Sunflowers			91.2	91.2	
13 14	Dry common beans (*phaseolus vulgaris* varieties only such as pinto, black, great northern, red, pink and navy)			45.6	45.6	1
13 14	Desi and Kabuli chickpeas			45.6	45.6	1
13	Alfalfa, seedling		Ground	91.2	91.2	[1]
14	Blueberry, highbush (Minor use)		Ground Application as a broadcast spray directed to the ground	91.2	91.2	1

USCs[1]	Site(s)[2]	Weeds	Application Method and Equipment	Maximum Application Rate (g ai/ha)		Maximum Number of Application Per Year
				Single[3]	Cumulative Per Year[3]	
14	Coriander (Minor use)		Ground	91.2	91.2	1
14	Fenugreek (Minor use)		Ground	91.2	91.2	1
13 14	Dry onions (Minor use)	Grass weeds including foxtail (green, yellow), Persian darnel, wild oats, volunteer cereals (wheat, barley, oats), barnyard grass, witchgrass, fall panicum, proso millet, volunteer corn, volunteer canary grass, quackgrass and annual bluegrass (suppression)	Ground	91.2	91.2	1
7 14	Prairie carnation – Alberta, Saskatchewan and Manitoba only (Minor use)	Grass weeds including foxtail (green, yellow), Persian darnel, wild oats, volunteer cereals (wheat, barley, oats), barnyard grass, witchgrass, fall panicum, proso millet, volunteer corn, volunteer canary grass, quackgrass	Ground	45.6	45.6	1
14	Spinach (Minor use)		Ground	45.6	91.2	2
7 14	Safflower (Minor use)		Ground	91.2	91.2	1
14	Cranberry (Minor use)		Ground	91.2	91.2	1

1. USCs 1 to 14 belong to the use sector AGRICULTURE AND FORESTRY.
2. Sites are as either stated on the label or interpreted by PMRA so as to achieve consistency in naming.
3. Rates of active ingredient (a.i.) were calculated by the PMRA. Note that the cumulative a.i. rate per year specified on the labels is 90 g a.i./ha when the cumulative product rate per year is 0.38 L/ha.

Appendix III Toxicology Endpoints for Health Risk Assessments

Table 1 Toxicity profile of clethodim

Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted. Effects seen above the LOAEL(s) have not been reported in this table for most studies for reasons of brevity.

Study Type/Animal/PMRA #	Study Results
Toxicokinetics Absorption, Distribution, Metabolism and Excretion - Sprague-Dawley rats gavage PMRA #1227015, 1232651	After 7 days the total amount of radiolabel recovered from organs and tissues in each of the dose groups, low, high and repeat dose, was less than 1% of the administered dose. The concentration in the tissues was adrenals > liver > kidney > bone, spinal cord, followed by the remaining tissues. Excretion of the ^{14}C-label was rapid and complete in the urine (87.2-93.2%), feces (9.3-17.0%) and carbon dioxide (0.5-1.0%); most (93.5-98.2%) was eliminated within 48 h. The major metabolite of ^{14}C clethodim was clethodim sulfoxide; in addition, smaller amounts of clethodim, clethodim sulfone, imine sulfoxide and 5-OH sulfone were present in the tissues. A metabolic pathway was suggested in which clethodim is rapidly oxidized to clethodim sulfoxide. Clethodim sulfoxide can be further oxidized to clethodim sulfone, deoxyalkylated to the imine sulfoxide or hydroxylated at the 5-position of the ring to yield 5-OH sulfoxide or 5-OH sulfone.
Acute oral toxicity gavage CD1 mice PMRA #1229860, 1229861	LD_{50} (♂) = 2570 mg/kg bw LD_{50} (♀) = 2430 mg/kg bw Signs: hypoactivity, rough coat, hunched posture, ataxia, urine stains, tremors, salivation Necropsy: in mice that died: slightly dark-red lungs, compound like material in the GI tract (no abnormalities noted in surviving mice) **low toxicity**
Acute oral toxicity gavage Sprague-Dawley rats PMRA #1229862, 1232654	LD_{50} (♂) = 1630 mg/kg bw LD_{50} (♀) = 1360 mg/kg bw Signs: Day 1: salivation, ↓motor activity, clonic convulsions, tremoring and/or unsteady gait, hyperactivity, collapse. Day 2-6 in survivors: ↓food consumption, yellow anogenital staining.

Study Type/Animal/PMRA #	Study Results
	Necropsy: dark gelatinous material beneath the meninges, mottled/reddened lungs, foam in the trachea, very small lesions of gliosis in a single spinal nerve in lower lumbar area in 2 \/s at 1.45 g/kg bw. **slightly toxic**
Acute dermal toxicity New Zealand White rabbits PMRA #1229863, 1232667	LD_{50} > 5000 mg/kg bw Signs: dermal effects included abraded, thickened, blackened/darkened, crusty and/or cracked skin. One male showed reduced food intake, decreased motor activity, decreased body temperature, unkempt appearance, diarrhea, no feces and collapse before dying on day 6. **low toxicity**
Acute inhalation toxicity Sprague-Dawley rats PMRA #1229864, 1232669	LC_{50} >3.9 mg/L Signs: salivation, red nasal discharge, abnormal respiratory sounds, mydriasis, decreased feces, unkempt appearance, yellow/red anogenital discharge **low toxicity**
Eye irritation New Zealand White rabbits PMRA #1229865, 1232670	MIS: 11.7 (1h unwashed); 10.7 (1h washed) MAS: 3.0 (unwashed); 0.43 (washed) All eyes were clear of irritation at 72h in the unwashed eyes, 48h in the washed **mild eye irritant**
Dermal irritation New Zealand White rabbits PMRA #1229866, 1232671	MIS(intact): (Trial 1) 1.75 (72h); (Trial 2) 0.25 (48h) MAS(intact): (Trial 1) 1.17; (Trial 2) 0.17 **mild dermal irritant**
Dermal sensitization (modified Buehler) Hartley Guinea pig PMRA #1229868, 1232673	**non-sensitizer**

Study Type/ Animal/PMRA #	Study Results
4-week dermal toxicity study Sprague-Dawley rats PMRA #1227481	**Systemic** **NOAEL = 100 mg/kg bw/day** **LOAEL = 1000 mg/kg bw/day** based on ↑urogenital discharge, ↓bw gain (♂: -35.2%), ↓bw (♂: -6.9%), ↑liver wt (♀) **Dermal** **NOAEL not determined** **LOAEL = 10 mg/kg bw/day** based on skin irritation There was a dose-related skin irritation in treated animals
4-week feeding study CD-1 mice PMRA #1229869, 1231831, 1231977	**NOAEL = 111 mg/kg bw/day (625 ppm)** **LOAEL = 274 mg/kg bw/day (1500 ppm)** based on ↓RBC (♂,♀-this dose only), ↓Hgb (♂,♀-this dose only), ↑liver wt (♂) No analysis of serum chemistry was performed
5-week feeding study Sprague-Dawley rats PMRA #1229870-1	**NOAEL = 65.6/78.6 mg/kg bw/day (1000 ppm)** **LOAEL = 261/291 mg/kg bw/day (4000 ppm)** based on ↓food consumption (wk 1 only), ↓bw, ↓bw gain, ↑liver wt., centrilobular hypertrophy (trace to mild), ↓Hct (♂), ↑uric acid (♀)
13-week feeding study Sprague-Dawley rats PMRA #1229872-4, 1229882, 1232674	**NOAEL (♂) = 25 mg/kg bw/day (500 ppm)** **NOAEL (♀) = 159 mg/kg bw/day (2500 ppm)** **LOAEL (♂) = 134/159 mg/kg bw/day (2500 ppm)** based on ↑liver wt, centrilobular hypertrophy of liver, ↑incidence of focal regeneration of the kidney, ↓bw (♂) **LOAEL (♀) = 279/341 mg/kg bw/day (5000 ppm)** based on ↓food consumption , ↑organ wt. (rel. - brain, kidney), ↑cholesterol (♂), ↑total protein (♂), ↑globulin (♂), ↓bw (♀) In animals recovering for 6 weeks, bwg was greater than controls but bw remained less than control wt. Organ wts. following recovery were generally similar to controls. No focal regeneration in the kidney, or liver hypertrophy was present in the recovery groups.
3-month feeding study	**NOAEL = 62.5 mg/kg bw/day** **LOAEL = 104 mg/kg bw/day** based on ↑liver wt. (absol.), ↑severity of cytoplasmic vesiculation/vacuolation of the central lobular hepatocytes,

Study Type/ Acceptable/Guideline #	Study Results
Beagle dogs PMRA #1229893, 1231833	↑globulin (♂), ↓albumin/globulin (♂), ↑ALP (♂)
1-year feeding study Beagle dogs PMRA #1229901	**NOAEL = 0.8 mg/kg bw/day*** **LOAEL = 62.5 mg/kg bw/day** based on ↑liver wt., hypercellularity of the bone marrow (1/6 ♂, 1/6 ♀), ↑polymorphic neutrophils (♂), ↑platelets (♂), ↓glucose (♂), ↑spleen pigment (♂). *based on the 90-day dog study the NOAEL could be set at 20.8 mg/kg bw/day. There were minor effects at 62.5 mg/kg bw/day in both studies and a large gap to the next lower dose in the 1-year study suggesting a NOAEL for the 1-year study of 20.8 mg/kg bw/day (in other words, the next lower dose in the 90-day study) would be appropriate.
18-month feeding study CD - 1 mice PMRA #1226180, 1226185, 1226186, 1226187, 1226188, 1226982, 1231837, 1234279	**NOAEL = 19.5/25.3 mg/kg bw/day (200 ppm)** **LOAEL ≥106/143 mg/kg bw/day (1000 ppm)** based on ↓survival, ↑multifocal, amphophilic alveolar lung macrophages, ↑centrilobular hypertrophy, ↑pigment in liver, ↑bile duct hyperplasia, ↑liver weight (♂- liver/body wt. and liver/brain wt. at wk. 53). **not carcinogenic**
2-year feeding study Sprague-Dawley rats PMRA #1227371-7, 1227379, 1227381, 1227451, 1227453-9, 1230580, 1230582-5	**NOAEL = 16 mg/kg bw/day (500 ppm)** **LOAEL = 86/113 mg/kg bw/day (2500 ppm)** based on ↓bw, ↑liver weight, ↑incidence of chronic pancreatitis, slight ↑incidence of binucleated cells of the liver. No treatment-related increase in tumours **not carcinogenic**
Dietary 2-generation reproductive study Sprague-Dawley rats PMRA #1227382, 1227383, 1227384, 1227385,1227386, 1227387, 1227388, 1227389, 1227390, 1227391, 1227399, 1234281	**Parental** **NOAEL = 28 mg/kg bw/day (500 ppm)** **LOAEL = 148 mg/kg bw/day** (2500 ppm) based on ↓bw (♂- F_1 & F_{2a}, ♀ - F_1), ↓fc (occasional) **Offspring** **NOAEL ≥148 mg/kg bw/day (2500 ppm)** **LOAEL not established** 148 mg/kg bw/day (2500 ppm): ↓pup bw (F_{1a}→F_{2a} generation, slight during lactation [not statistically significant and considered non-adverse]

Study Type/ Guideline/ PMRA #s	Study Results
	Reproductive **NOAEL** ≥ 949 mg/kg bw/day (≥7500 ppm) **LOAEL not established** No treatment-related effects were observed.
Developmental toxicity study gavage CD rats PMRA #1229881, 1229825, 1230978, 1230979, 1236262	**Maternal** **NOAEL** = 100 mg/kg bw/day **LOAEL** = 350 mg/kg bw/day based on clinical signs (↑incidence of excessive salivation, red nasal discharge, staining of fur in the ano-genital region), ↓bw, ↓uterine wt **Developmental** **NOAEL** = 100 mg/kg bw/day **LOAEL** = 350 mg/kg bw/day based on ↓fetal bw, ↑skeletal variations (*delayed ossification*) **Malformations at doses exceeding MTD**
Developmental toxicity study gavage New Zealand White rabbits PMRA #1229837, 1229840, 1229859	**Maternal** **NOAEL** = 83 mg/kg bw/day **LOAEL** = 249 mg/kg bw/day based on ↓bw, ↓bwg, ↓fc and food utilization (days 7-20), ↑incidence dried feces and red substance in pan (*thought to be due to GI irritation rather than abortion*) **Developmental** **NOAEL** ≥249 mg/kg bw/day **LOAEL not established** 249 mg/kg bw/day: slight ↑skeletal variations (non-adverse)
Ames test *S. typhimurium* TA98, TA100, TA1535, TA1537, *E. coli* WP2 uvrA PMRA #1229479, 1229649	negative
Ames test	negative

Study Type, test system [PMRA #]	Study Results
In vivo micronucleus (5 hr/48, 5 hr/48, 3 hr/2x24, 5 hr/2x24) [PMRA # 4137241/01, 4137242]	
Chromosome aberrations in CHO cells Chinese Hamster Ovary (CHO) Cells [PMRA # 4137241/02, 4137242]	positive w/o activation only Positive when tested in the absence of metabolic activation. A significant increase in the frequency of structural chromosome aberrations per cell was observed at 1.0 and 1.2 µL/mL. No significant increase was seen in either structural aberrations per cell in the activated system or in numerical aberrations for either test system
Chromosome aberrations in CHO cells Chinese Hamster Ovary (CHO) Cells [PMRA # 4240622]	negative Negative with and without metabolic activation (1.2 µL/mL). This is a repeat of the above using a much purer form of the technical. An impurity seems likely responsible for the positive effect noted above.
In vivo chromosome aberration assay Sprague-Dawley rat bone marrow [PMRA # 4137241/03, 4137242]	negative
Unscheduled DNA Synthesis Hepatocytes of BNL 3B1 mice [PMRA # 4137241/04, 4137242]	negative
Acute oral neurotoxicity study Wistar rats [PMRA # 4137240, 4137242]	NOAEL = 100 mg/kg bw LOAEL = 1000 mg/kg bw based on ↓bwg, ↓spontaneous activity, hunched posture, ruffled fur, ↑nerve fibre degeneration of the ventral lumbar cord, abnormal gait (♂), ↑salivation (♂), head tilt (♂)

Study Type/Animal/PMRA #	Study Results
28-day oral (dietary) range-finding neurotoxicity study Sprague-Dawley rats PMRA #2308446	♂45/51 mg/kg bw/day (500 ppm): ↓bwg; ↓bw (♂) ♀132/155 mg/kg bw/day (1500 ppm): ↑liver weight (♀) No neurotoxic potential was indicated up to the highest dose-levels tested (441/475 mg/kg bw/day). This study was used to establish the doses in the main 90-day neurotoxicity study
90-day oral (dietary) neurotoxicity study Sprague-Dawley rats PMRA #2308444	**NOAEL = 94/115 mg/kg bw/day** **LOAEL = 331/380 mg/kg bw/day (5000 ppm)** based on ↓bw, ↑liver weight
28-day oral (dietary) range-finding immunotoxicity study. B6C3F1 mice PMRA #2308448	♀551 mg/kg bw/day (2000 ppm): ↑liver weight
28-day oral (dietary) immunotoxicity study. B6C3F1 mice PMRA #2308450	**NOAEL = 136 mg/kg bw/day** **LOAEL = 603 mg/kg bw/day (2000 ppm)** based on ↑liver weight, slight ↓spleen weight, slight ↓spleen cells, slight ↓specific activity AFC's, slight ↓total spleen activity AFC's **Equivocal evidence for immunotoxicity**
Plant Metabolites: Imino sulfone (RE-47719) acute oral toxicity gavage Sprague-Dawley rats PMRA #1227466	LD_{50} (♀) > 1400 mg/kg bw One animal had ↓motor activity 4 hours after dosing and was found dead the following morning. All other animals appeared normal. Necropsy: small intestine of animal that died contained red gelatinous material. The results suggest that imino sulphone is less acutely toxic than clethodim to the ♀ rat.
Plant Metabolites:	1) 5-OH sulfone: 1400 mg/kg bw: no mortality, or clinical signs of

Study Type/Animal/PMRA #	Study Results
5-OH sulfone (RE-51228) vs. clethodim (RE-45601) acute oral toxicity gavage Sprague-Dawley rats PMRA #1227467	toxicity, ↑bw during the 14 day post-treatment period, no gross tissue abnormalities (LD_{50} (♀) > 1400 mg/kg bw). 2) clethodim: 1400 mg/kg bw: severe signs of toxicity (salivation, decreased motor activity, collapse, hyperactivity, tremors, ↓fc, diarrhoea, dehydration and nasal, ocular, oral and ano-genital discharges), all animals died within 3 days, ↓bw day 0-2, necropsy showed red discolored lungs, blood pooled beneath the cranial meninges and black discolored spleen, gastric mucosa, intestine and caecum 5-OH sulphone is considerably less toxic than clethodim.
Plant Metabolites: Imine sulfone (RE-47719) 5-week oral (dietary) toxicity study Sprague-Dawley rats PMRA #1227357	**NOAEL = 70.9 mg/kg bw/day (1000 ppm)** **LOAEL = 604/723 mg/kg bw/day (8000 ppm)** based on ↑cholesterol, ↑liver wt. ; ↓bwg (♂- wk. 1), ↓fc (♂- wk. 1), ↑reticulocytes (♂)
Plant Metabolites: 5-OH sulfone (RE-51228) 5-week oral (dietary) toxicity study Sprague-Dawley rats PMRA #1227358	**NOAEL ≥588 mg/kg bw/day (8000 ppm)** **LOAEL not established** No toxic effects were observed
Plant Metabolites: Imine sulfone (RE-47719) Developmental toxicity study gavage Sprague Dawley rats PMRA #1227359	**Maternal** ≥100 mg/kg bw/day: ↓bwg 700 mg/kg bw/day: clinical signs (excessive salivation), ↓fc (during dosing), **Developmental** 700 mg/kg bw/day: ↓bw, ↑incidence of fetal variations [↑cervical rib present (per litter); ↓average number of sternal centers (ossification sites per fetus per litter)] **Supplementary** (screening; n=10)

Study Type/Animal/PMRA #	Study Results
Plant Metabolites: 5-OH sulfone (RE-51228) Developmental toxicity study gavage Sprague Dawley rats PMRA #1227360	**Maternal** 700 mg/kg bw/day: clinical signs (rales, excessive salivation) **Developmental** 5-OH sulfone was not toxic to the fetus **Supplementary** (screening; n=10)
Plant Metabolites: Imine sulfone (RE-47719) Ames test S. typhimurium TA98, TA100, TA1535, TA1537, E. coli WP2 uvrA PMRA #1227361	**negative**
Plant Metabolites: Imine sulfone (RE-47719) Chromosome aberrations in CHO cells Chinese Hamster Ovary (CHO) Cells PMRA #1227362	**negative**
Plant Metabolites: 5-OH sulfone (RE-51228) Ames test S. typhimurium TA98, TA100, TA1535, TA1537, E. coli WP2 uvrA PMRA #1229446	**negative**

Study Type/Animal/PMRA #	Study Results
Plant Metabolites: 5-OH sulfone (RE-51228) Chromosome aberrations in CHO cells Chinese Hamster Ovary (CHO) Cells PMRA #1229458	**negative**

Table 2 Toxicology Endpoints for Use in Health Risk Assessment for Clethodim

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute dietary	Acute oral neurotoxicity study - rats	NOAEL = 100 mg/kg bw Clinical signs of toxicity: reduced activity, hunched posture, abnormal gait, salivation, head tilt	100
	ARfD = 1.0 mg/kg bw		
Chronic dietary	2-year dietary study in the rat	NOAEL = 16 mg/kg bw/day Liver toxicity, ↓bw, ↑incidence of chronic pancreatitis	100
	ADI = 0.16 mg/kg bw/day		
Short/Intermediate-term inhalation[2]	90-day dietary rat	NOAEL = 25 mg/kg bw/day ↓bw, kidney effects, ↑liver wt., hepatocellular hypertrophy	100
Short/Intermediate-term dermal	28-day dermal rat	NOAEL = 100 mg/kg bw/day ↓bw, ↑liver wt., urogenital discharge	100
Cancer	No evidence of carcinogenicity		

[1] CAF (composite assessment factor) refers to a total of uncertainty and *Pest Control Products Act* factors for dietary assessments; MOE refers to a target MOE for occupational assessments.
[2] An oral NOAEL was selected, and an inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation.

Appendix IV Agricultural Mixer/Loader/Applicator and Postapplication Risk Assessment

Table 1 Occupational Mixer/Loader/Applicator Exposure and Risk Assessment (Baseline PPE)

Crop	Application Equipment	Scenario	ATPD[a]	Application Rate[b]	MOE (Target = 100)		
					Dermal[c]	Inhalation[d]	Combined[e]
Canola, flax, lentil, mustard, pea, potato, soybean, sunflower	Groundboom	Farmer	107 ha	91.2 g ai/ha	9800	80,000	8730
		Custom	360 ha		2910	23,800	2600
	Aerial	Mixer/loader	400 ha		4290	34,300	3810
		Applicator			22,700	783,000	22,100
Chickpea	Groundboom	Farmer	107 ha	45.6 g ai/ha	19,600	160,000	17,500
		Custom	360 ha		5830	47,600	5200
	Aerial	Mixer/loader	400 ha		8580	68,500	7600
		Applicator			45,400	1,570,000	44,100
Alfalfa seedling, safflower	Groundboom	Farmer	107 ha	91.2 g ai/ha	9800	80,000	8730
		Custom	360 ha		2910	23,800	2600
Beans (dry)	Groundboom	Farmer and Custom	26 ha	45.6 g ai/ha	80,700	659,000	71,900
	Aerial	Mixer/loader	400 ha		8580	68,500	7620
		Applicator			45,400	1,570,000	44,100
Coriander, fenugreek, onions	Groundboom	Farmer and Custom	26 ha	91.2 g ai/ha	40,300	329,000	35,900
Prairie carnation, spinach	Groundboom	Farmer and Custom	26 ha	45.6 g ai/ha	80,700	659,000	71,900
Blueberry (high bush)	Groundboom	Farmer and Custom	26 ha	91.2 g ai/ha	40,300	329,000	35,900
	LPHW		1.5 ha		62,000	323,000	52,000
	Backpack				10,700	235,000	10,300
Cranberry	Groundboom[f]	Farmer and Custom	107 ha	91.2 g ai/ha	9800	80,000	8730
	HPHW		35 ha		455	4200	410
	LPHW		1.5 ha		68,200	356,000	57,200
	Backpack				11,800	259,000	11,300

ATPD = area treated per day, LPHW = manually pressurized handwand, HPHW = mechanically pressurized handgun

[a] Default areas from the PMRA ATPD table were used. For handheld equipment, the default values for amount handled per day (L/ha) were converted to areas using the minimum spray volume on the label (100 L/ha for blueberries and 110 L/ha for cranberries).

[b] Maximum label application rate

[c] Dermal MOEs are based on a dermal NOAEL of 100 mg/kg bw/day. Target is 100. Dermal MOE = NOAEL/ (Unit Exposure (µg/kg ai) * ATPD * Application Rate / Body Weight (80 kg)). Unit exposure values are from PHED.

[d] Inhalation MOEs are based on an oral NOAEL of 25 mg/kg bw/day. Target is 100. Inhalation MOE = NOAEL/ (Unit Exposure (µg/kg ai) * ATPD * Application Rate / Body Weight (80 kg)). Unit exposure values are from PHED.

[e] Calculated using the following equation: Combined MOE = $1/(1/MOE_{dermal})+(1/MOE_{inhalation})$).

[f] Groundboom included as potential application equipment in the minor use assessment.

Table 2 Postapplication Exposure and Risk Assessment

Crop	TC [a] (cm^2/hr)	Application Rate [b]	Day 0		
			DFR[c] (µg/cm^2)	Exposure[d] (mg/kg bw/day)	MOE[e] (Target = 100)
Alfalfa seedling, high bush blueberry, lentil, coriander, fenugreek, mustard, pea, potato, safflower	1750	91.2 g ai/ha	0.228	0.0180	2510
Chickpea, bean	1750	45.6 g ai/ha	0.114	0.00898	5010
Spinach	1750	45.6 g ai/ha (two apps)[f]	0.140	0.0110	4080
Flax, soybean, canola, cranberry	1100	91.2 g ai/ha	0.228	0.0113	4000
Prairie carnation	1100	45.6 g ai/ha	0.114	0.00564	7970
Onion	4400	91.2 g ai/ha	0.228	0.0451	997
Sunflower	90	91.2 g ai/ha	0.228	0.000923	48,700

[a] TC = transfer coefficient. The highest TC for each crop was included in this table. See Table 3 below for a list of the activities and additional TCs for each crop.
[b] Maximum label application rate
[c] DFR = dislodgeable foliar residue. The default peak DFR value of 25% of the application rate was assumed.
[d] Dermal exposure = TC * DFR * 8 hours / Body Weight (80 kg).
[e] MOE = margin of exposure. MOE = NOAEL/exposure. Dermal MOEs are based on a dermal NOAEL of 100 mg/kg bw/day. Target is 100.
[f] Two applications, 14 days apart. The default 10% dissipation rate was assumed.

Table 3 Summary of Transfer Coefficient for Clethodim

Crop	Activity	TC (cm^2/hr)
Alfalfa seedling, bean (dry), pea (field), lentil[a]	Irrigation (hand set)	1750
	Scouting	1100
	Mechanical harvesting, mechanical swathing (beans, peas), mechanical knifing (beans, peas), mechanical weeding (beans, peas), fertilizing, irrigation (non-hand set)	0
Canola, flax, prairie carnation[b]	Scouting	1100
	Mechanical harvesting, irrigation (non-hand set)	0
Soybean	Scouting	1100
	Hand weeding	70
	Mechanical harvesting, mechanical weeding (soybean), mechanical swathing (buckwheat), bailing straw (buckwheat), irrigation (non-handset)	0
Chickpea, safflower	Irrigation (hand set)	1750
	Scouting	1100
	Hand weeding	70
	Mechanical harvesting, mechanical knifing, mechanical swathing, mechanical weeding, fertilizing, irrigation (non-hand set)	0
Coriander[c], fenugreek[c], mustard, spinach	Irrigation (hand set)	1750
	Hand harvesting	1100
	Hand weeding	70
	Scouting	210
	Transplanting	230
	Mechanical harvesting, mechanical weeding, irrigation (non-hand set)	0
Sunflower	Scouting, bird control	90
	Mechanical harvesting	0
Onion (dry)	Hand weeding	4400

Table 3 Summary of Transfer Coefficient for Clethodim

Crop	Activity	TC (cm^2/hr)
	Irrigation (hand set)	1750
	Scouting, thinning	1300
	Mechanical harvesting, mechanical weeding, irrigation (non-hand set)	0
Potato	Irrigation (hand set)	1750
	Roguing	1000
	Scouting	210
	Hand weeding	70
	Mechanical harvesting, mechanical weeding, irrigation (non-hand set)	0
Blueberry (high bush)	Irrigation (hand set)	1750
	Hand pruning, scouting, bird control, hand weeding, frost control	640
	Transplanting	230
	Mechanical harvesting, mechanical weeding, irrigation (non-hand set)	0
Cranberry	Hand harvesting (raking), scouting	1100
	Transplanting	230
	Hand pruning (shears), hand weeding	70
	Mechanical harvesting (flood), mechanical weeding, sanding, ditching, frost control, irrigation (non-hand set)	0

TC = transfer coefficient

[a] Beans(dry) were used as a surrogate crop for lentils

[b] Canola was used as surrogate crop for prairie carnation

[c] Parsley was used as a surrogate crop for coriander and fenugreek

Appendix V Dietary Exposure and Risk Estimates for Clethodim

Table 1 Summary of Acute Dietary Exposure and Risk from Clethodim

Population Subgroup	Acute Dietary (95th percentile)[1]			
	Food only		Food + Water	
	Exposure (mg/kg bw)	%ARfD	Exposure (mg/kg bw)	%ARfD
General Population	0.034374	3.44	0.035492	3.55
All Infants	0.057396	5.74	0.060795	6.08
Children 1-2 years old	0.070148	7.01	0.071939	7.19
Children 3-5 years old	0.067183	6.72	0.069079	6.91
Children 6-12 years old	0.042608	4.26	0.043691	4.37
Youth 13-19 years old	0.025700	2.57	0.026494	2.65
Adults 20-49 years old	0.023880	2.39	0.024942	2.49
Adults 50-99 years old	0.023018	2.30	0.023917	2.39
Females 13-49 years old	0.023884	2.39	0.025101	2.51

[1]Acute Reference Dose (ARfD) of 1 mg/kg bw.

Table 2 Summary of Chronic Dietary Exposure and Risk from Clethodim

Population Subgroup	Chronic Dietary[1]			
	Food only		Food + Water	
	Exposure (mg/kg bw/day)	%ADI	Exposure (mg/kg bw/day)	%ADI
General Population	0.013072	8.2	0.013930	8.7
All Infants	0.025133	15.7	0.027347	17.1
Children 1-2 years old	0.037578	23.5	0.038817	24.3
Children 3-5 years old	0.031078	19.4	0.032121	20.1
Children 6-12 years old	0.019182	12.0	0.019935	12.5
Youth 13-19 years old	0.010942	6.8	0.011568	7.2
Adults 20-49 years old	0.010470	6.5	0.011327	7.1
Adults 50-99 years old	0.010172	6.4	0.011018	6.9
Females 13-49 years old	0.010321	6.5	0.011174	7.0

[1]Acceptable Daily Intake (ADI) of 0.16 mg/kg bw/day.

Table 3 Dietary Input Characterization for Clethodim

Food Commodity	Residues	Source
Alfalfa, seed	0.1	CDN GMRL
Amaranth, Leafy	2	US Tolerance for subgroup 4A
Arrowroot, flour	1	US Tolerance for subgroup 1C
Artichoke, globe	1.2	US Tolerance
Arrowroot, flour-babyfood	1	US Tolerance for subgroup 1C
Artichoke, Jerusalem	1	US Tolerance for subgroup 1C
Arugula	2	US Tolerance for subgroup 4A
Asparagus	1.7	US Tolerance
Balsam pear	0.5	US Tolerance for subgroup 9B
Basil, dried leaves	12	US Tolerance for subgroup 19A
Basil, dried leaves-babyfood	12	US Tolerance for subgroup 19A

Food Commodity	Residues	Source
Basil, fresh leaves	12	US Tolerance for subgroup 19A
Basil, fresh leaves-baby food	12	US Tolerance for subgroup 19A
Bean, black, seed	1.5	US Tolerance for group 6
Bean, broad, succulent	1.5	US Tolerance for group 6
Bean, broad, seed	1.5	US Tolerance for group 6
Bean, cowpea, succulent	1.5	US Tolerance for group 6
Bean, cowpea, seed	1.5	US Tolerance for group 6
Bean, great northern, seed	1.5	US Tolerance for group 6
Bean, kidney, seed	1.5	US Tolerance for group 6
Bean, lima, succulent	1.5	US Tolerance for group 6
Bean, lima, seed	1.5	US Tolerance for group 6
Bean, mung, seed	1.5	US Tolerance for group 6
Bean, navy, seed	1.5	US Tolerance for group 6
Bean, pink, seed	1.5	US Tolerance for group 6
Bean, pinto, seed	1.5	US Tolerance for group 6
Bean, snap, succulent	1.5	US Tolerance for group 6
Bean, snap, succulent-baby food	1.5	US Tolerance for group 6
Beef, meat	0.2	US Tolerance
Beef, meat-baby food	0.2	US Tolerance
Beef, meat, dried	0.2	US Tolerance
Beef, meat byproducts	0.2	US Tolerance
Beef, meat byproducts-baby food	0.2	US Tolerance
Beef, fat	0.2	US Tolerance
Beef, fat-baby food	0.2	US Tolerance
Beef, kidney	0.2	US Tolerance
Beef, liver	0.2	US Tolerance
Beef, liver-baby food	0.2	US Tolerance
Beet, garden, roots	1	US Tolerance for subgroup 1B
Beet, garden, roots-baby food	1	US Tolerance for subgroup 1B
Beet, sugar	0.2	US Tolerance
Beet, sugar-baby food	0.2	US Tolerance
Beet, sugar, molasses	1	US Tolerance
Beet, sugar, molasses-baby food	1	US Tolerance
Blackberry	0.3	US Tolerance for subgroup 13-07A
Blackberry, juice	0.3	US Tolerance for subgroup 13-07A
Blackberry, juice-baby food	0.3	US Tolerance for subgroup 13-07A
Blueberry	0.2	CDN MRL
Blueberry-baby food	0.2	CDN MRL
Broccoli	3	US Tolerance for subgroup 5A
Broccoli-baby food	3	US Tolerance for subgroup 5A
Broccoli, Chinese	3	US Tolerance for subgroup 5A
Broccoli raab	3	US Tolerance for subgroup 5B
Brussels sprouts	3	US Tolerance for subgroup 5A
Burdock	1	US Tolerance for subgroup 1B
Cabbage	3	US Tolerance for subgroup 5A
Cabbage, Chinese, bok choy	3	US Tolerance for subgroup 5B
Cabbage, Chinese, napa	3	US Tolerance for subgroup 5A
Cabbage, Chinese, mustard	3	US Tolerance for subgroup 5A
Cantaloupe	2	US Tolerance for subgroup 9A
Cardoon	0.6	US Tolerance for subgroup 4B
Carrot	1	US Tolerance for subgroup 1B
Carrot-baby food	1	US Tolerance for subgroup 1B
Carrot, juice	1	US Tolerance for subgroup 1B

Food Commodity	Residues	Source
Cassava	1	US Tolerance for subgroup 1C
Cassava-baby food	1	US Tolerance for subgroup 1C
Cauliflower	3	US Tolerance for subgroup 5A
Celeriac	1	US Tolerance for subgroup 1B
Celery	0.6	US Tolerance for subgroup 4B
Celery-baby food	0.6	US Tolerance for subgroup 4B
Celery, juice	0.6	US Tolerance for subgroup 4B
Celtuce	0.6	US Tolerance for subgroup 4B
Chayote, fruit	0.9	US Tolerance for subgroup 9B
Chicken, meat	0.2	US Tolerance
Chicken, meat-baby food	0.2	US Tolerance
Chicken, liver	0.2	US Tolerance
Chicken, meat byproducts	0.2	US Tolerance
Chicken, meat byproducts-baby food	0.2	US Tolerance
Chicken, fat	0.2	US Tolerance
Chicken, fat-baby food	0.2	US Tolerance
Chicken, skin	0.2	US Tolerance
Chicken, skin-baby food	0.2	US Tolerance
Chickpea, seed	3.5	US Tolerance for group 6
Chickpea, seed-baby food	3.5	US Tolerance for group 6
Chickpea, flour	3.5	US Tolerance for group 6
Chicory, roots	1	US Tolerance for subgroup 1B
Chinese waxgourd	0.5	US Tolerance for subgroup 9B
Chrysanthemum, garland	2	US Tolerance for subgroup 4A
Collards	3	US Tolerance for subgroup 5B
Coriander, seed	3	CODEX
Coriander, seed-baby food	3	CODEX
Corn, field, flour	0.2	US Tolerance
Corn, field, flour-baby food	0.2	US Tolerance
Corn, field, meal	0.2	US Tolerance
Corn, field, meal-baby food	0.2	US Tolerance
Corn, field, bran	0.2	US Tolerance
Corn, field, starch	0.2	US Tolerance
Corn, field, starch-baby food	0.2	US Tolerance
Corn, field, syrup	0.2	US Tolerance
Corn, field, syrup-baby food	0.2	US Tolerance
Corn, field, oil	0.2	US Tolerance
Corn, field, oil-baby food	0.2	US Tolerance
Corn, pop	0.2	US Tolerance
Cottonseed, oil	0.5	CODEX
Cottonseed, oil-baby food	0.5	CODEX
Cranberry	0.5	CDN MRL
Cranberry-baby food	0.5	CDN MRL
Cranberry, dried	0.5	CDN MRL
Cranberry, juice	0.5	CDN MRL
Cranberry, juice-baby food	0.5	CDN MRL
Cress, garden	2	US Tolerance for subgroup 4A
Cress, upland	2	US Tolerance for subgroup 4A
Cucumber	0.5	US Tolerance for subgroup 9B
Currant	0.2	CDN MRL
Currant, dried	0.2	CDN MRL
Dandelion, leaves	2	US Tolerance for subgroup 4A
Dasheen, corm	1	US Tolerance for subgroup 1C

Food Commodity	Residues	Source
Dill, seed	15	U.S. Tolerance for subgroup 19A
Dillweed	15	U.S. Tolerance for subgroup 19A
Egg, whole	0.2	U.S. Tolerance
Egg, whole-baby food	0.2	U.S. Tolerance
Egg, white	0.2	U.S. Tolerance
Egg, white (solids)-baby food	0.2	U.S. Tolerance
Egg, yolk	0.2	U.S. Tolerance
Egg, yolk-baby food	0.2	U.S. Tolerance
Eggplant	1	U.S. Tolerance for group 8
Elderberry	0.2	CODEX MRL
Endive	7	U.S. Tolerance for subgroup 4A
Fennel, Florence	0.6	U.S. Tolerance for subgroup 4D
Flax seed, oil	0.6	U.S. Tolerance
Garlic, bulb	0.5	CODEX
Garlic, bulb-baby food	0.5	CODEX
Ginger	1	U.S. Tolerance for subgroup 1C
Ginger-baby food	1	U.S. Tolerance for subgroup 1C
Ginger, dried	1	U.S. Tolerance for subgroup 1C
Ginseng, dried	1	U.S. Tolerance for subgroup 1D
Goat, meat	0.2	U.S. Tolerance
Goat, meat by-products	0.2	U.S. Tolerance
Goat, fat	0.2	U.S. Tolerance
Goat, kidney	0.2	U.S. Tolerance
Goat, liver	0.2	U.S. Tolerance
Gooseberry	0.2	CODEX MRL
Guava	0.2	CODEX MRL
Guava-baby food	0.2	CODEX MRL
Herbs, other	15	U.S. Tolerance for Herb subgroup 19A
Herbs, other-baby food	15	U.S. Tolerance for Herb subgroup 19A
Honeydew melon	2	U.S. Tolerance for subgroup 9A
Hop	0.5	U.S. Tolerance
Horse, meat	0.2	U.S. Tolerance
Horseradish	1	U.S. Tolerance for subgroup 1D
Huckleberry	0.2	CODEX MRL
Kale	5	U.S. Tolerance for subgroup 5D
Kohlrabi	5	U.S. Tolerance for subgroup 5A
Lentil, seed	0.5	U.S. Tolerance for group 6
Lettuce, head	2	U.S. Tolerance for subgroup 4A
Lettuce, leaf	2	U.S. Tolerance for subgroup 4A
Loganberry	0.5	U.S. Tolerance for subgroup 13-07A
Meat, game	0.2	CODEX
Milk, fat	0.1	CODEX (MRL)
Milk, fat-baby food/infant formula	0.1	CODEX (MRL)
Milk, nonfat solids	0.1	CODEX (MRL)
Milk, nonfat solids-baby food/infant formula	0.1	CODEX (MRL)
Milk, water	0.1	CODEX (MRL)
Milk, water-baby food/infant formula	0.1	CODEX (MRL)
Milk, sugar (lactose)-baby food/infant formula	0.1	CODEX (MRL)
Mustard greens	5	U.S. Tolerance for subgroup 5D
Onion, bulb	0.2	CODEX MRL
Onion, bulb-baby food	0.2	CODEX MRL
Onion, bulb, dried	0.2	CODEX MRL
Onion, bulb, dried-baby food	0.2	CODEX MRL

Food Commodity	Residues	Source
Onion, green	2	US Tolerance
Parsley, turnip rooted	1	US Tolerance for subgroup 1B
Parsnip	1	US Tolerance for subgroup 1B
Parsnip baby food	1	US Tolerance for subgroup 1B
Pea, dry	1.5	US Tolerance for group 6
Pea, dry baby food	1.5	US Tolerance for group 6
Pea, pigeon, seed	1.5	US Tolerance for group 6
Peach	0.2	US Tolerance
Peach baby food	0.2	US Tolerance
Peach, dried	0.2	US Tolerance
Peach, dried baby food	0.2	US Tolerance
Peach, juice	0.2	US Tolerance
Peach, juice baby food	0.2	US Tolerance
Peanut	5	US Tolerance
Peanut, butter	5	US Tolerance
Peanut, oil	5	US Tolerance
Pepper, bell	1	US Tolerance for group 4
Pepper, bell baby food	1	US Tolerance for group 4
Pepper, bell, dried	1	US Tolerance for group 4
Pepper, bell, dried baby food	1	US Tolerance for group 4
Pepper, nonbell	1	US Tolerance for group 4
Pepper, nonbell baby food	1	US Tolerance for group 4
Pepper, nonbell, dried	1	US Tolerance for group 4
Peppermint	9	US Tolerance
Peppermint, oil	9	US Tolerance
Pork, meat	0.2	US Tolerance
Pork, meat baby food	0.2	US Tolerance
Pork, skin	0.2	US Tolerance
Pork, meat byproducts	0.2	US Tolerance
Pork, meat byproducts baby food	0.2	US Tolerance
Pork, fat	0.2	US Tolerance
Pork, fat baby food	0.2	US Tolerance
Pork, kidney	0.2	US Tolerance
Pork, liver	0.2	US Tolerance
Potato, chips	0.5	CODEX MRL
Potato, dry (granules/flakes)	2	US Tolerance
Potato, dry (granules/flakes) baby food	2	US Tolerance
Potato, flour	0.5	CODEX MRL
Potato, flour baby food	0.5	CODEX MRL
Potato, tuber, w/peel	0.5	CODEX MRL
Potato, tuber, w/peel baby food	0.5	CODEX MRL
Potato, tuber, w/o peel	0.5	CODEX MRL
Potato, tuber, w/o peel baby food	0.5	CODEX MRL
Poultry, other, meat	0.2	US Tolerance
Poultry, other, liver	0.2	US Tolerance
Poultry, other, meat byproducts	0.2	US Tolerance
Poultry, other, fat	0.2	US Tolerance
Poultry, other, skin	0.2	US Tolerance
Pumpkin	0.5	US Tolerance for subgroup 9B
Pumpkin, seed	0.5	US Tolerance for subgroup 9B
Rabbit, meat	0.2	CODEX
Radicchio	2	US Tolerance for subgroup 1A
Radish, roots	1	US Tolerance for subgroup 1B

Food Commodity	Residues	Source
Radish, tops	0.7	U.S Tolerance
Radish, Oriental, roots	1	U.S Tolerance for wilgroup 1B
Rape greens	7	U.S Tolerance for wilgroup 5B
Rapeseed, oil	0.5	U.S Tolerance
Rapeseed, oil/fatty/food	0.5	U.S Tolerance
Raspberry	0.5	U.S Tolerance for wilgroup 13-07F
Raspberry, fatty/food	0.5	U.S Tolerance for wilgroup 13-07F
Raspberry, juice	0.5	U.S Tolerance for wilgroup 13-07F
Raspberry, juice fatty/food	0.5	U.S Tolerance for wilgroup 13-07F
Rutabaga	0.6	U.S Tolerance for wilgroup 1B
Rutabaga	1	U.S Tolerance for wilgroup 1B
Safflower, oil	2	U.S Tolerance
Safflower, oil/fatty/food	2	U.S Tolerance
Salsify, roots	1	U.S Tolerance for wilgroup 1B
Sesame, seed	0.05	U.S Tolerance
Sesame, seed/fatty/food	0.05	U.S Tolerance
Sesame, oil	0.05	U.S Tolerance
Sesame, oil/fatty/food	0.05	U.S Tolerance
Sheep, meat	0.2	U.S Tolerance
Sheep, meat/fatty/food	0.2	U.S Tolerance
Sheep, meat byproducts	0.2	U.S Tolerance
Sheep, fat	0.2	U.S Tolerance
Sheep, fat/fatty/food	0.2	U.S Tolerance
Sheep, kidney	0.2	U.S Tolerance
Sheep, liver	0.2	U.S Tolerance
Soybean, seed	10	CDN VRL
Soybean, flour	10	CDN VRL
Soybean, flour/fatty/food	10	CDN VRL
Soybean, soy milk	10	CDN VRL
Soybean, soy milk/fatty/food or infant formula	10	CDN VRL
Soybean, oil	10	CDN VRL
Soybean, oil/fatty/food	10	CDN VRL
Spearmint	8	U.S Tolerance
Spearmint, oil	8	U.S Tolerance
Spices, other	0.7	CDN VRL for Fenugreek, seed
Spices, other/fatty/food	0.7	CDN VRL for Fenugreek, seed
Spinach	3	CDN VRL
Spinach/fatty/food	3	CDN VRL
Squash, summer	0.5	U.S Tolerance for wilgroup 9B
Squash, summer/fatty/food	0.5	U.S Tolerance for wilgroup 9B
Squash, winter	0.5	U.S Tolerance for wilgroup 9B
Squash, winter/fatty/food	0.5	U.S Tolerance for wilgroup 9B
Strawberry	5	U.S Tolerance
Strawberry, fatty/food	5	U.S Tolerance
Strawberry, juice	5	U.S Tolerance
Strawberry, juice fatty/food	5	U.S Tolerance
Sunflower, seed	5	U.S Tolerance
Sunflower, oil	5	U.S Tolerance
Sunflower, oil/fatty/food	5	U.S Tolerance
Sweet potato	1	U.S Tolerance for wilgroup 1C
Sweet potato fatty/food	1	U.S Tolerance for wilgroup 1C
Swiss chard	0.6	U.S Tolerance for wilgroup 4B
Tomato, corn	1	U.S Tolerance for wilgroup 1C

Food Commodity	Residues	Source
Tomatillo	1	US Tolerance for group 8
Tomato	1	US Tolerance for group 8
Tomato-baby food	1	US Tolerance for group 8
Tomato, paste	1	US Tolerance for group 8
Tomato, paste-baby food	1	US Tolerance for group 8
Tomato, puree	1	US Tolerance for group 8
Tomato, puree-baby food	1	US Tolerance for group 8
Tomato, dried	1	US Tolerance for group 8
Tomato, dried-baby food	1	US Tolerance for group 8
Tomato, juice	1	US Tolerance for group 8
Turkey, meat	0.2	US Tolerance
Turkey, meat-baby food	0.2	US Tolerance
Turkey, liver	0.2	US Tolerance
Turkey, liver-baby food	0.2	US Tolerance
Turkey, meat by products	0.2	US Tolerance
Turkey, meat by products-baby food	0.2	US Tolerance
Turkey, fat	0.2	US Tolerance
Turkey, fat-baby food	0.2	US Tolerance
Turkey, skin	0.2	US Tolerance
Turkey, skin-baby food	0.2	US Tolerance
Turnip, tops	4	US Tolerance for subgroup 1C
Turnip, roots	1	US Tolerance for subgroup 1B
Turnip, greens	1	US Tolerance for subgroup 5B
Water, direct, all sources	0.041	PMRA #2414981
Water, indirect, all sources	0.041	PMRA #2414981
Watermelon	2	US Tolerance for subgroup 9A
Watermelon, juice	2	US Tolerance for subgroup 9A
Yam, true	1	US Tolerance for subgroup 1C
Yam bean	1	US Tolerance for subgroup 1C

Appendix VI Food Residue Chemistry Summary

Clethodim, a member of the cyclohexanedione family of herbicide, was evaluated by the JMPR in 1994, 1997, 1999 and 2002.

Clethodim is currently registered in Canada for post-emergent control of a number of grasses and weeds on various terrestrial feed and food crops, and for industrial oil seed and fibre crops. Registered clethodim end-use products are formulated as emulsifiable concentrates or emulsion, to be applied by ground or aerial equipment.

The nature of the residue in livestock and plant commodities is adequately understood based on metabolism studies in goats, laying hens, soybeans, carrots, and cotton. In Canada, the residue definition in plant and animal commodities is currently expressed as the parent clethodim and metabolites containing the 2-cyclohex-1-enone moiety.

Clethodim shares a common moiety with sethoxydim, another herbicide currently registered in Canada. This common moiety accounts for the major part of their structures, which differ in two parts: the oxime oxygen bears an ethyl group in sethoxydim but a 3-chloroallyl group in clethodim, and the imino carbon bears an n-propyl group in sethoxydim but an ethyl group in clethodim. Sethoxydim has been re-evaluated under Re-evaluation Program 1 (PRVD2007-17; RVD2008-10) and granted continued registration.

Analytical methods have been previously reviewed by the PMRA. The common moiety method RM-26A (PMRA# 1232663) has been used to analyse clethodim residues in plant and animal matrices. Method RM-26A and modifications thereof were deemed adequate for data gathering.

RM-26A-1 and RM-26B-3 are enforcement methods for plant and animal matrices. However, RM-26B-3 cannot distinguish between residues of clethodim (and its metabolites) and sethoxydim (and its metabolites). These methods were used by independent laboratories and considered to have been successfully validated. Additionally, a method specific to clethodim is listed under the U.S. FDA's Pesticide Analytical Manual Volume II.

Overall, available field trial data for registered crops support the established MRLs. However, confined crop rotation data on file are inadequate to support the establishment of plant back intervals. Therefore, a restriction against crop rotation should be added to clethodim labels.

Appendix VII Supplemental Maximum Residue Limit Information – International Situation and Trade Implications

Maximum residue limits (MRLs) may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data. For animal commodities, differences in MRLs can be due to different livestock feed items and practices.

Table 1 Comparison between MRLs in Canada and in Other Jurisdictions

Crop	Canadian MRL (ppm)	U.S. Tolerance (ppm)	Codex MRL (ppm)
Alfalfa, fodder	-	-	10
Alfalfa, forage	-	6	-
Alfalfa, hay	-	10	-
Alfalfa, Seedling	*	-	-
Aronia berries	0.2	0.2	-
Artichoke, globe	-	1.2	-
Asparagus	-	1.7	-
Beans	0.5	-	-
Beans, dry	-	2.5	2
Bean, fodder	-	-	10
Beans, except broad bean and soybean	-	-	0.5
Bearberries	0.5	-	-
Beet, fodder	-	-	0.1
Beet, sugar	-	-	0.1
Beet, sugar, molasses	-	1	-
Beet, sugar, roots	-	0.2	-
Beet, sugar, tops	-	1	-
Bilberries	0.5	-	-
Brassica, head and stem, subgroup 5A *(includes broccoli, broccoli Chinese, brussels sprouts, cabbage except Chinese bok choy cabbage, cauliflower, kohlrabi)*	-	3	-
Brassica, leafy greens, subgroup 5B *(includes broccoli raab, Chinese bok choy cabbage, collards, kale, mustard greens, rape greens, turnip greens)*	-	3	-

Crop	Canadian MRL (ppm)	U.S. Tolerance (ppm)	Codex MRL (ppm)
Caneberry subgroup 13-07A *(includes blackberry, loganberry, black, red and wild raspberry)*	-	0.3	-
Cattle, fat	-	0.2	-
Cattle, meat	-	0.2	-
Cattle, meat byproducts	-	0.2	-
Chilean guavas	0.2	0.2	-
Cloudberries	0.5	-	-
Clover, forage	-	10	-
Clover, hay	-	20	-
Coriander seeds	3	-	-
Corn, field, forage	-	0.2	-
Corn, field, grain	-	0.2	-
Corn, field, stover	-	0.2	-
Cotton, meal	-	2	-
Cotton, undelinted seed	-	1	-
Cotton, seed	-	-	0.5
Cotton seed oil, Crude	-	-	0.5
Cotton seed oil, Edible	-	-	0.5
Cranberries	0.5	0.5	-
Currants	0.2	0.2	-
Currants, Buffalo	0.2	0.2	-
Dry chickpeas	0.5	-	-
Dry lentils	0.5	-	-
Dry peas	0.5	-	2
Edible offal (mammalian)	-	-	0.2
Eggs	-	0.2	0.05
Elderberries	0.2	0.2	-
European barberries	0.2	0.2	-
Fenugreek seeds	0.7	-	-
Flax, meal	-	1	-
Flaxseeds	0.3	0.6	-
Garlic	-	-	0.5
Goat, fat	-	0.2	-
Goat, meat	-	0.2	-
Goat, meat byproducts	-	0.2	-
Gooseberries	0.2	0.2	-
Herb subgroup 19A *(includes basil, dillweed)*	-	12	-
Highbush blueberries	0.2	0.2	-

Crop	Canadian MRL (ppm)	U.S. Tolerance (ppm)	Codex MRL (ppm)
Highbush cranberries	0.2	0.2	-
Hog, fat	-	0.2	-
Hog, meat	-	0.2	-
Hog, meat byproducts	-	0.2	-
Honeysuckle	0.2	0.2	-
Hop, dried cones	-	0.5	-
Horse, fat	-	0.2	-
Horse, meat	-	0.2	-
Horse, meat byproducts	-	0.2	-
Huckleberries	0.2	0.2	-
Jostaberries	0.2	0.2	-
Leaf petioles subgroup 4B *(includes cardoon, celery, celtuce, florence fennel, rhubarb, swiss chard)*	-	0.6	-
Leafy greens subgroup 4A *(includes, amaranth, arugula, chervil, chrysanthemum edible-leaved, chrysanthemum garland, cress garden, cress upland, dandelion, endive, lettuce leaf ,lettuce head, parsley, radicchio, spinach)*	-	2	-
Lingonberries	0.5	0.2	-
Lowbush blueberries	0.2	0.2	-
Meat (from mammals other than marine mammals)	-	-	0.2
Melon subgroup 9A *(includes cantaloupe, honeydew melon, watermelon)*	-	2	-
Milk	-	0.05	0.05
Muntries	0.5	-	-
Mustard seeds (condiment type)	0.4	-	-
Mustard seeds (oilseed type)	0.05	0.5	-
Mustard, Yellow	*	-	-
Onion, bulb	0.2	0.2	0.5
Onion, green	-	2	-
Partridgeberries	0.5	-	-
Peach	-	0.2	-
Peanut	-	3	5
Peanut, hay	-	3	-
Peanut, meal	-	5	-

Crop	Canadian MRL (ppm)	U.S. Tolerance (ppm)	Codex MRL (ppm)
Peppermint, tops	-	5	-
Potatoes	0.5	0.5	0.5
Potato, granules/flakes	-	2	-
Poultry, fat	-	0.2	-
Poultry, meat	-	0.2	0.2
Poultry, meat byproducts	-	0.2	-
Poultry, Edible offal of	-	-	0.2
Prairie Carnation	N/A	-	-
Radish, tops	-	0.7	-
Rapeseeds (canola, seed)	0.05	0.5	0.5
Canola, meal	-	1	-
Rapeseed oil, Crude	-	-	0.5
Rapeseed oil, Edible	-	-	0.5
Safflower, seed	*	5	-
Safflower, meal	-	10	-
Salal berries	0.2	0.2	-
Saskatoon berries (juneberries)	0.2	0.2	-
Sea buckthorn	0.2	0.2	-
Sesame, seed	-	0.35	-
Sheep, fat	-	0.2	-
Sheep, meat	-	0.2	-
Sheep, meat byproducts	-	0.2	-
Soybean (Dry)	10	10	10
Soyabean oil, Crude	-	-	1
Soyabean oil, Refined	-	-	0.5
Spearmint, tops	-	5	-
Spinach	2	2	-
Squash/cucumber subgroup 9B *(includes chayote fruit, Chinese waxgourd, cucumber, balsam apple, balsam pear, pumpkin, squash)*	-	0.5	-
Strawberry	-	3	-
Sunflower, meal	-	10	-
Sunflower, seeds	0.2	5	0.5
Sundflower seed oil, Crude	-	-	0.1
Tomato	-	1	1
Vegetable, fruiting group 8 *(include eggplant, pepper, tomatillo, tomato)*	-	1	-
Vegetable, legume, group 6, except soybean	-	3.5	-

Crop	Canadian MRL (ppm)	U.S. Tolerance (ppm)	Codex MRL (ppm)
(include succulent and dried peas, beans)			
Vegetable, root, except sugar beet, subgroup 1B *(includes garden beet, burdock, carrot, celeriac, chicory, ginseng, horseradish, parsley, parsnip, radish, radish oriental, rutabaga, salsify, turnip)*	-	1	-
Vegetable, tuberous and corm, subgroup 1C *(includes arrowroot, artichoke Jerusalem, cassava, chayote (root), dasheen, ginger, potato, sweet potato, tanier, turmeric, yam bean, yam true)*	-	1	-

*No MRLs were specified for the following registered crops: alfalfa seedling, mustard yellow and safflower. Residues in/on these crops are covered under Part B, Division 15, subsection B.15.002(1) of the *Food and Drug Regulations* as 0.1 ppm.

- Canadian MRLs website: http://pr-rp.hc-sc.gc.ca/mrl-lrm/index-eng.php
- CODEX MRLs website: http://www.codexalimentarius.net/pestres/data/index.html?lang=en
- U.S. Tolerances website: http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&tpl=/ecfrbrowse/Title40/40cfr180_main_02.tpl

Table 2 Residue Definition in Canada and Other Jurisdictions

Jurisdiction	Residue Definition	
Canada	Current	2-[1-[[[(2E)-3-chloro-2-propen-1-yl]oxy]imino]propyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one, including metabolites containing the 2-cyclohex-1-enone moiety
	Proposed	**Sum of clethodim** [(±) -2-[(E)-3-chloroallyoxyimino]propyl]-5-[2-(ethylthio)propyl]-3-hydroxycyclohex-2-enone)] and its metabolites containing the 2-cyclohex-1-enone moiety, **expressed as clethodim**
United States		2-[(1E)-1-[[[(2E)-3-chloro-2-propenyl]oxy]imino]propyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one, and its metabolites containing the 5-(2-ethylthiopropyl)cyclohexene-3-one and 5-(2-ethylthiopropyl)-5-hydroxycyclohexene-3-one moieties and their sulphoxides and sulphones, calculated as the stoichiometric equivalent of clethodim, in or on the commodity
Codex (JMPR)		Sum of clethodim and its metabolites containing 5-(2-ethylthiopropyl)cyclohexene-3-one and 5-(2-ethylthiopropyl)-5-hydroxycyclohexene-3-one moieties and their sulphoxides and sulphones, expressed as clethodim

Appendix VIII Environmental Risk Assessment

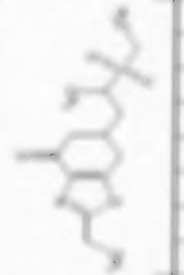
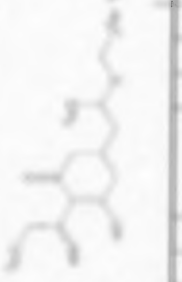
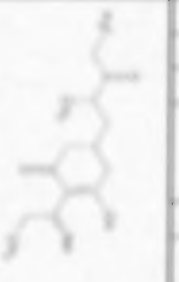
Table 1 Physical and chemical properties of clethodim

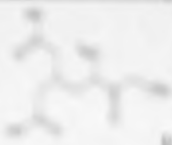
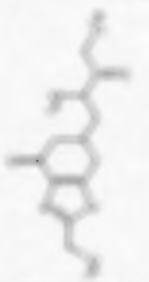
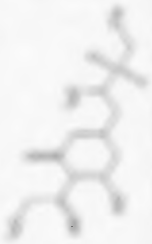
Property	Result[a]	Comment
Vapour pressure at 20°C	$< 1 \times 10^{-7}$ mPa	Low vapour pressure, not likely to volatilize from soil or water surfaces
Henry's law constant at 20°C	$1.01 \times 3.7 \times 10^{-9}$ (Evaluator calculated)	Low potential for volatilization from water and moist soil
Ultraviolet (UV) / visible spectrum	pH λ_{max} (nm) Neutral: 203, 256, 283 Acidic: 207, 258, 261 Basic: 210, 282, 283 *No absorbance at $\lambda > 350$ nm*	Low potential for direct photoransformation
Solubility in water at 20°C	pH 4.2 13.0 (mg/L) 7 5.45 g/L 9 58.9 g/L[b]	Soluble at acidic pH; very soluble at neutral and alkalin pHs (Solubility is dependent on pH)
Solubility (g/L) in organic solvents at 25 °C	Soluble in most organic solvents Solvent — Solubility (g/L) Acetone > 900 Ethyl acetate > 900 Hexane > 900 Dimethylformamide > 900 Methanol > 1000	Generally soluble in most organic solvents
n-Octanol/water partition coefficient (Log Kow & Kow) at 20°C	pH Log Kow Kow 5.35 4.4 2.5×10^4 7 4.14 1.38×10^4	Potential for bioaccumulation
Dissociation constant	4.16	Weak acid
Stability (temperature, metal)	The half-life of Clethodim Technical was estimated to be about 9 months at 21-23°C; the rate of decomposition was estimated to be at about 5.4% per month. Thermally unstable; 47.2% loss after 14 days at 54°C in the dark.	

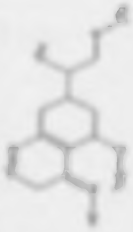
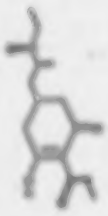
[a] Data obtained from Chemistry Review, PMRA 2320917, 2324667
[b] PMRA 2416284

Table 2 Table of maximum formation of transformation products

Code	Chemical name	Chemical structure	Study	max %AR (day)	%AR at Study End (study length)
MAJOR (>10% TB AND/OR MEI) TRANSFORMATION PRODUCTS					
RE-47365	Clothianidin Oxazole		Aerobic soil		
			Anaerobic soil		
			Soil photolysis		
			Aqueous photolysis	DT50 14.2 (2.5) [sing-6-e](pH5.5	DT50 14.2 (2.5) [sing-6-e](pH5.5
			Hydrolysis	50(5.32) pH5.5 50 (29 mins) pH9.0	50 (5.32) pH5.5 50 (29 mins) pH9.0
			Aerobic aquatic	10.6 (3)	0 (182)
			Anaerobic aquatic	1.2 (101)	
			Field studies		
RE-46261	3-chloro-allyl alcohol		Aerobic soil		
			Anaerobic soil		
			Soil photolysis		
			Aqueous photolysis	DT50 31.3 (15) [AS] pH5.7	DT50 29.2 (30) [AS] pH5.7
			Hydrolysis	20.7(30) pH5.5	30.7(30) pH5.5
			Aerobic aquatic		
			Anaerobic aquatic		
			Field studies		
	3-chloroprop-enal		Aerobic soil		
			Anaerobic soil		
			Soil photolysis		
			Aqueous photolysis	DT50 31.3 (2.5) [AS] pH5.5	DT50 31.3 (2.5) [AS] pH5.5
			Hydrolysis		
			Aerobic aquatic		
			Anaerobic aquatic		
			Field studies		
RE-45924	Clothianidin sulfonate		Aerobic soil	7.8(3)	1.1(121)
			Anaerobic soil	20(1)	1.3(30)
			Soil photolysis		
			Aqueous photolysis	DT50 14.2 (3) [sing-6-e] pH5.7 DT50 57.3 (3) [sing-6-e] pH5.7 DT50 14.2 (3) [AS] pH5.7 DT50 32.7 (1) [AS] pH5.7	DT50 5.7 (30) [sing-6-e](pH5.7 DT50 6.0 (30) [AS] pH5.7 DT50 25.6 (1.25) [AS] pH5.7
			Hydrolysis		
			Aerobic aquatic	22.6 (1) whole system	1.9 (196)

Code	Chemical name	Chemical structure	Study	mean $\%\lambda$DT (days)	$\%\lambda$DT or Study End (days) [days]
				[illegible]	
			Anaerobic aquatic		
			Field studies		
BE-47205	Clothodim sulfone		Aerobic soil	[illegible]	[illegible]
			Anaerobic soil		
			Soil photolysis		
			Aqueous photolysis		
			Hydrolysis		
			Aerobic aquatic	[illegible] whole system [illegible] (water)	[illegible]
			Anaerobic aquatic	[illegible]	
			Field studies		
BE-47707	Clothodim oxazole sulfone		Aerobic soil	[illegible]	[illegible]
			Anaerobic soil		
			Soil photolysis		
			Aqueous photolysis		
			Hydrolysis		
			Aerobic aquatic	[illegible] (water)	
			Anaerobic aquatic	[illegible] (water)	[illegible] (water)
			Field studies		
BE-47686	Clothodim imine		Aerobic soil		
			Anaerobic soil	[illegible]	[illegible]
			Soil photolysis		
			Aqueous photolysis	DT [illegible] (pH [illegible] [illegible] pH [illegible]	DT [illegible] (pH [illegible] [illegible] pH [illegible]
			Hydrolysis	[illegible] (pH [illegible] mean) pH [illegible]	[illegible] (pH [illegible] mean) pH [illegible]
			Aerobic aquatic	[illegible] (DT [illegible]) whole	[illegible] (DT [illegible])
			Anaerobic aquatic		
			Field studies		
BE-47708	Clothodim imine sulfoxide		Aerobic soil	[illegible] (DT [illegible])	
			Anaerobic soil		
			Soil photolysis		
			Aqueous photolysis	DT [illegible] (pH [illegible] [illegible] pH [illegible] pH [illegible] (pH [illegible] [illegible] pH [illegible]	DT [illegible] (pH [illegible] [illegible] pH [illegible] pH [illegible] (pH [illegible] [illegible] pH [illegible]
			Hydrolysis		
			Aerobic aquatic	[illegible] (DT [illegible]) whole system [illegible] (sediment)	[illegible] (DT [illegible])
			Anaerobic aquatic	[illegible] (DT [illegible])	[illegible] (DT [illegible])
			Field studies		
			Other		

Code	Chemical name	Chemical structure	Study	mean % (SD) (days)	% (SD) at study end (study length)
BE-[illegible]	[illegible]		Aerobic soil		
			Anaerobic soil		
			Soil photolysis		
			Aqueous photolysis	DT50 = 48.3 (1.30) [time, h; r) pH 7 DT50 = 55.3 (1.3) [time, h; r) pH 9	DT50 = 48.3 (1.30) [time, h; r) pH 7 DT50 = 55.3 (1.3) [time, h; r) pH 9
			Hydrolysis		
			Aerobic aquatic		
			Anaerobic aquatic		
			Field studies		
	[illegible]		Aerobic soil		
			Anaerobic soil		
			Soil photolysis		
			Aqueous photolysis	DT50 = 13.8 (1.25) [time, h; r) pH 7 DT50 = 11.7 (1.3) [time, h; r) pH 9	DT50 = 9.7 (1.30) [time, h; r) pH 7 DT50 = 8.1 (1.3) [time, h; r) pH 9
			Hydrolysis		
			Aerobic aquatic		
			Anaerobic aquatic		
			Field studies		
[illegible]					
BE-[illegible]	[illegible]		Aerobic soil	4.0 (35)	
			Anaerobic soil		
			Soil photolysis		
			Aqueous photolysis	DT50 = 8.5 (1.3) [time, h; r) pH 9	DT50 = 8.5 (1.3) [time, h; r) pH 9
			Hydrolysis	1.3 (1.3) [time, h; pH 9	
			Aerobic aquatic	0.2 (water)	
			Anaerobic aquatic	0.5 (120) [time, water	7.3 (365)
			Field studies		
BE-[illegible]	[illegible]		Aerobic soil		
			Anaerobic soil		
			Soil photolysis		
			Aqueous photolysis		
			Hydrolysis		
			Aerobic aquatic	0.5 (sediment)	
			Anaerobic aquatic	0.2 (42)	
			Field studies		
			Other		
BE-[illegible]			Aerobic soil	2.1 (3)	
			Anaerobic soil		

Code	Chemical name	Chemical structure	Study	mean %AR (day)	%AR at Study End (study length)
			Soil photolysis		
			Aqueous photolysis	DR: ~4.5 (1.5) [mmp-4-c] pH5.5	DR: ~4 (2) [mmp-4-c] pH5.5
	Clethodim mixture		Hydrolysis		
			Aerobic aquatic	9.7 (0.25) water	0.0 (196)
			Anaerobic aquatic	1.2 (101)	
			Field studies		
	(±)-2-[1-[2-hydroxy-6-methoxy-4-[1-methyl-2-(methylthio)ethyl] cyclohex-1-ene carbonyl]		Aerobic soil		
			Anaerobic soil		
			Soil photolysis		
			Aqueous photolysis		
			Hydrolysis	2.1 (19 mins)	1.5 (29 mins)
			Aerobic aquatic		
			Anaerobic aquatic		
			Field studies		
BE-07586	Triton Sulfoxide		Aerobic soil		
			Anaerobic soil		
			Soil photolysis		
			Aqueous photolysis	SR: ~7.5 (0.5) [mmp-4-c] pH5.5	SR: ~2 (2.5) [mmp-4-c] pH5.5
			Hydrolysis		
			Aerobic aquatic		
			Anaerobic aquatic		
			Field studies		

D = dark control, IR = irradiated, SS= Sensitized and irradiated (sensitized by the addition of acetone), AR = Applied Radioactivity

Table 3 Fate and behaviour in the environment of clethodim technical grade active ingredient and its major transformation products clethodim sulfoxide, clethodim sulfone, clethodim oxazole sulfone and clethodim imine

Property	Test substance	Value	Transformation products	Comments	Reference
Abiotic transformation					
Hydrolysis	clethodim	25°C IPVI EPA pH 5, DT_{50}: 26 d; pH 7, DT_{50}: 900 d; pH 9, DT_{50}: 300 d 25°C IPVI Environment Canada pH 5, DT_{50}: 28 d; pH 7, DT_{50}: 900 d; pH 9, DT_{50}: 310 d	Major: Clethodim oxazole 3-chloro-allyl-alcohol Chloropropanal-3-ol Clethodim imine	Hydrolysis can contribute to dissipation of clethodim especially in acidic conditions.	1226985 1074744

		25°C [All] pH 5, DT_{50}: 42 d; pH 7, DT_{50}: 360 d; 25°C [ring-6] pH 4, DT_{50}: 0.76 d; pH 7, DT_{50}: 31.3 d; pH 9, DT_{50}: stable 35°C [ring-6] pH 4, DT_{50}: 0.53 d; pH 7, DT_{50}: 0.56 d; pH 9, DT_{50}: stable			
Phototransformation on soil	clethodim	DT_{50} (irradiated): 1.52-1.82 d; DT_{50} (dark): 1.87-1.96 d A phototransformation half-life could not be calculated as dissipation was similar in the dark controls.	Major, Irradiated: Clethodim sulfoxide Major, Dark: Clethodim sulfoxide Minor, Irradiated: CO_2 Minor, Dark: CO_2	Photolysis is not an important route of dissipation for clethodim in the terrestrial environment.	1226988
Biotransformation					
Biotransformation in aerobic soil	clethodim	Sandy loam soil at 25°C **[ring-4,6-14C]:** DT_{50}: 1.23 d; DT_{90}: 4.09 d **[allyl-14C]:** DT_{50}: 1.19 d; DT_{90}: 3.94d **[propyl-^{14}C]:** DT_{50}: 2.47 d; DT_{90}: 8.19 d Combined labels: DT_{50}: 1.58 d; DT_{90}: 5.24 d	Major: Clethodim sulfoxide, clethodim sulfone, CO_2, clethodim oxazole sulfone, Minor: Clethodim oxazole Clethodim oxazole sulfoxide, clethodim oxazole sulfone, Clethodim imine sulfoxide	clethodim is non-persistent	1226990; 1234277; 1226991
	Clethodim sulfoxide:	**[ring-4,6]:** DT_{50}: 15.4 d; DT_{90}: 59.4 d ; $t_{0.5,0.02}$= 17.9 **[allyl]:** DT_{50}: 18.2 d; DT_{90}: 60.4 d **[propyl]:** DT_{50}: 24.7 d; DT_{90}: 81.9		Clethodim sulfoxide is slightly persistent	

		d Combined labels: DT_{50}: 19.9 d; DT_{90}: 66.3 d			
	Clethodim sulfone	[propyl]: DT_{50}: 22.1 d; DT_{90}: 101 d ; $f_{n\ max}$= 30.3		Clethodim sulfone is slightly persistent.	
	Clethodim oxazole sulfone	[propyl]: DT_{50} could not be determined as residues were formed late in the study and was accumulating at the end of the study at 380 days.		Clethodim oxazole sulfone may be persistent in aerobic soil	
Biotransformation in anaerobic soil	Clethodim	Sandy loam: DT_{50}: 63.7 d; DT_{90}: 212 d	Minor: Organic volatiles CO_2 Unknown	Clethodim is moderatley-persistent	1371483
	Clethodim sulfoxide:	DT_{50}: 8.13 d; DT_{90}: 27 d		Clethodim sulfoxide is non persistent	
	Clethodim imine	DT_{50} could not be determined as concentrations continued to accumulate at study termination		Clethodim imine maybe prescistent in anaerobic soil	
Mobility					
Adsorption / desorption in soil **Koc** mobility classification based on McCall *et alet al* (1981	Clethodim	Five U.S. soils: Dallas, Clay loam (pH 8.1, 2.8% OM) K_d: 0.13; K_{OC}: 7.8 Bertie, Loamy sand (pH 5.8, 1.0% OM) K_d: 1.73; K_{OC}: 298.3 Attus, Sand (pH 7.8, 1.3% OM) K_d: 0.51; K_{OC}: 67.4 Stephenville, Sandy clay loam (pH 7.0, 0.6% OM) K_d: 0.32; K_{OC}: 91.2 Fresno, Loamy sand (pH 7.0, 0.4% OM) K_d: 0.26; K_{OC}: 112.8 Three other soils: Gleissolo Melanico Aluminico inceptico (GMa) (pH 4.0, 33% OM) K_d: 8.61; K_{OC}: 44.97 Latossolo Vermelho Distroferrico tipico (LVdf) (pH 4.7, 3.8% OM) K_d: 1.57; K_{OC}: 71.3		Low to very high mobility in soils.	1226989, 1074746

		Latossolo Vermelho Distroferrico psamitico (**LVd**) (pH 5.3, 2% OM) K_d: 0.87; K_{OC}: 74.72		
	Clethodim sulfoxide	Berty, loamy sand (pH 5.8, 1.0% OM) K_d: 0.26; K_{OC}: 44.48	Very high mobility in soil	
	Clethodim sulfone	Berty, loamy sand (pH 5.8, 1.0% OM) K_d: 0.11; K_{OC}: 19.3		
	Clethodim oxazole sulfone	Five soils: Dallas, Clay loam (pH 8.1, 2.8% OM) K_d: 10.73; K_{OC}: 660.9 Bertie, Loamy sand (pH 5.8, 1.0% OM) K_d: 0.37; K_{OC}: 63.12 Attus, Sand (pH 7.8, 1.3% OM) K_d: 1.13; K_{OC}: 149.5 Stephenville, Sandy clay loam (pH 7.0, 0.6% OM) K_d: 1.65; K_{OC}: 475 Fresno, Loamy sand (pH 7.0, 0.4% OM) K_d: 2.21; K_{OC}: 951.9	Low to very high mobility in soils.	
Soil leaching	No acceptable study was submitted. Submitted studies and foreign reviews indicate a high potential for vertical mobility/leaching			1234274
Volatilization	Not required based on the low vapour pressure (1×10^{-2} mPa at 20°C) and Henry's law constant (6.6×10^{-7} Pa·m³/mol ; 1/H= 3.7×10^{3} at 20°C).			
Field studies				
Field dissipation in Canada	Clethodim as Select 2EC containing 0.24kg clethodim/L	10 bare plot sites DT_{90} could not be determined due to degradation of clethodim during storage. Deepest layer analyzed: 0-10 cm	Clethodim sulfoxide, Clethodim sulfone, Clethodim oxazole sulfoxide, Clethodim oxazole sulfone were detected at very low concentrations.	Data could not be interpreted due to instability of clethodim during storage.	1234270, 1150035, 1140881, 1229455

Aquatic systems					
Property	**Test substance**	**Value**	**Transformation products**	**Comments**	**Reference**
Abiotic transformation					
Hydrolysis	clethodim	25°C [Pr] pH 5, DT50: 26 d; pH 7, DT50: 300 d; pH 9, DT50: 300 d 25°C [Al]	Major: Clethodim oxazole (pH 5) 3-chloro-allyl-alcohol	Hydrolysis can contribute to the overall dissipation of clethodim, especially at acidic and neutral	1226985 1074744

		pH 5, DT50: 42 d; pH 7, DT50: 360 d; 25°C[ring-6] pH 4, DT50: 0.76 d; pH 7, DT50: 31.3 d; pH 9, DT50: stable 35°C[ring-6] pH 4, DT50: 0.53 d; pH 7, DT50: 0.56 d; pH 9, DT50: stable	Chloropropenal-3-ol Clethodim imine	pH.	
Phototransformation in water	[ring-4-6]-^{14}C clethodim	Dark system (D) DT_{50} (pH 5: 12.5 d; DT_{50} (pH 7): 99.4 d DT_{50} (pH 9): 330 d	Major : Dark Clethodim oxazole	Can be an important route of dissipation for clethodim and its transformation products in the environment	1226986
		Non-sensitized irradiated (IR) DT_{50} (pH 5: 1.7 d; DT_{50} (pH 7): 6.8 d DT_{50} (pH 9): 9.6d	Major,(IR): Clethodim sulfoxide, clethodim imine, clethodim imine sulfoxide, DME sulfoxide and imine ketone Minor, (IR) Trione sulfoxide, clethodim oxazole sulfoxide, CO_2, volatile organics and clethodim oxazole		
		Sensitized irradiated (SS) DT_{50} (pH 5: 0.94 d; DT_{50} (pH 7): 1.2 d DT_{50} (pH 9): 0.52 d	Major,(SS): Clethodim sulfoxide, clethodim imine, clethodim imine sulfoxide, DME sulfoxide **Note:** clethodim imine sulfoxide and DME sulfoxide were still accumulating in the environment at study end (30 d).		
	[Al]-^{14}C clethodim	Dark system (D) DT_{50} (pH 5): 20.1 d; DT_{50} (pH 7): 60.9 d	Major : Dark Chloroallyl alcohol Minor Dark Clethodim sulfoxide		1226987

		Non-sensitized irradiated (IR) DT_{50} (pH 5: 1.5 d; DT_{50} (pH 7): 4.1 d DT_{50} (pH 9): 6.0d	Major,(IR): Clethodim sulfoxide, chloroallyly alcohol and 3-chloropropenal **Note:** chloroallyly alcohol and 3-chloropropenal remained in stable concentration at study end (30 d).		
		Sensitized irradiated (SS) DT_{50} (pH 5): 0.20 d; DT_{50} (pH 7): 0.61 d DT_{50} (pH 9): 0.33 d	Major,(SS): Clethodim sulfoxide, chloroallyly alcohol and 3-chloropropenal CO_2 Minor, Irradiated: Volatile organics		
	Clethodim	Direct in ultrapure water DT_{50}: 28 mins; Indirect in the presence of (0.5 -20 mg/L) of humic acid, nitrates and Fe (III) ions: DT_{50}: 2.6 mins to 2.5 days	E-clethodim Ketone of clethodim imine Clethodim imine sulfoxide Clethodim sulfoxide Clethodim imine Z-Clethodim		2475150
Biotransformation					
Biotransformation in aerobic water-sediment systems	Clethodim	slough water: sandy clay loam sediment dark system at 25°C Whole system DT_{50}: 5.84 d; DT_{90}: 19.4 d light system at 25°C Whole system DT_{50}: 4.32 d; DT_{90}: 14.4 d dark system at 5°C Whole system DT_{50}: 9.6 d; DT_{90}: 155 d (slow $t_{1/2}$ = 62.8)	Major: Clethodim imine, Clethodim sulfoxide, clethodim sulfone and clethodim oxazole, CO_2 Minor: Volatile organics, clethodim imine sulfoxide, clethodim imine sulfone, clethodim oxazole sulfoxide and	Clethodim is non-persistent. Biotransformation in aerobic water-sediment systems is a route of dissipation for clethodim.	1234275

			clethodim oxazole sulfone.		
	clethodim	Pond water: loamy silt sediment at 20°C Whole system DT50: 23.6 d; DT90: 78.5 d	Major: **Water:** Clethodim sulfoxide **Sediment:** Clethodim imine, Clethodim imine sulfoxide, CO2 Minor: Volatile organics, clethodim oxazole, clethodim imine sulfone and clethodim sulfone	clethodim, clethodim sulfoxide and clethodim imine sulfoxide are moderately persistent	2416280
	Clethodim sulfoxide	Whole system DT50: 49.1 d; DT90: 163 d			
	Clethodim imine sulfoxide	Whole system DT50: 50.8 d; DT90: 169 d			
	Clethodim imine	DT_{50} could not be calculated as concentrations increased until study termination.		Clethodim imine may be persistent	
Biotransformation in anaerobic water-sediment systems	Clethodim	slough water: sandy clay loam sediment dark system at 25°C Whole system DT_{50}: 108 d; DT_{90}: 657 d DFOP(slow $t_{1/2}$ = 237) dark system at 5°C Whole system DT_{50}: 530 d; DT_{90}: 1760 d	Major: Clethodim imine and clethodim sulfoxide combined. DT_{50} could not be calculated as concentrations increased until study termination. Minor: **Aqueous** Clethodim oxazole sulfoxide, clethodim oxazole sulfone **sediment** clethodim imine sulfoxide, clethodim sulfone, clethodim imine sulfone, clethodim oxazole CO_2	Clethodim is moderately persistent Biotransformation in anaerobic water-sediment systems is a route of dissipation for clethodim.	1234276
Field studies					
Aquatic field dissipation	No aquatic field dissipation study with clethodim was submitted, and data on the aquatic field disspiation of clethodim are not required.				
Bioconcentration/bioaccumulation					
Bioconcentration in bluegill sunfish	[allyl] and [ring]-^{14}C clethodim at 0.05 mg/L (nominal concentration)	Whole fish steady state BCF: 2.1 for allyl] and [ring]-^{14}C clethodim	Clethodim sulfoxide	Did not bioconcentrate in large amounts in fish under the test conditions of the study.	1227461

Table 4 Toxicity of clethodim and transformation products to Non-Target terrestrial Species

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Invertebrates					
Earthworm, *Eisenia foetida*	14-d Acute	Clethodim Agan Technical (95.8%)	LC_{50}: 1767 mg a.i./kg soil	No classification	1074747
	14-d Acute	Clethodim sulfoxide	LC_{50}: >1000 mg/kg soil	No classification	2416283
	14-d Acute	Select (clethodim 240 EC) 28.4%.	LC_{50}: 454 mg/kg soil = 129 mg a.i/kg soil	No classification	1234271
	14-d Acute	Clethodim 240 CE (240 g/L)	LC_{50}: 353.55 mg/kg soil **= 84.8 mg a.i/kg soil**	No classification	1074729
Honeybee, *Apis mellifera*	48-h Oral	Clethodim Agan technical (95.8%)	**LD_{50}: 313 µg a.i./bee**	Relatively non-toxic	1074749
	72-h Oral	Select 240 EC 240g clethodim/L	LD_{50} >51 µg a.i./bee	Relatively non-toxic	2416283
	48-h Oral	Select 240 EC 240g clethodim/L	LD_{50} **>43 µg a.i./bee**	Relatively non-toxic	
		Mixture of Select + Para sommer 256 g clethodim/L	LD_{50} 55 µg a.i./bee	Relatively non-toxic	
	48-h Contact	Clethodim Agan technical (95.8%)	**LD_{50}: 37.29 µg a.i./bee**	Relatively non-toxic	1074748
		Clethodim 87.9%a.i.	LD_{50}: >100 µg a.i./bee	Relatively non-toxic	1227462
		Select 2.0 EC 25.6% .	LD_{50}:**> 33 µg a.i./bee**	Relatively non-toxic	2416283
		Select 240 EC 240g clethodim/L	LD_{50}:> 51 µg a.i./bee	Relatively non-toxic	
		Mixture of Select + Para sommer 256 g clethodim/L	LD_{50} 68 µg a.i./bee	Relatively non-toxic	
Parasitoid wasp, *Aphidius rhopalosiphi*	48h-Contact,	1:2 (v/v) mixtures of Select (25% clethodim/L) and Para Sommer (75% Paraffin oil)	**LR_{50}: >240 g a.i./ha**	No classification	2416283
Predatory mite, *Typhlodromus pyri*	14-d Contact, extended laboratory	1:2 (v/v) mixtures of Select (25% clethodim/L) and Para Sommer (75% Paraffin oil)	LR_{50}: <9.6 g a.i/ha	No classification	
Predatory mite,	14-d Contact,	1:2 (v/v)	**LR_{50}: 3.6 g a.i/ha**	No	

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Typhlodromus pyri	extended laboratory including 7 days fecundity assessment	mixtures of Select (25% clethodim/L) and Para Sommer (75% Paraffin oil)		classification	
Poecilus cupreus	14-d laboratory (sand)	1:2 (v/v) mixtures of Select (25% clethodim/L) and Para Sommer (75% Paraffin oil)	**LR_{50}: >256 g a.i/ha**	No classification	
	14-d laboratory (sand)	Select 240	**LR_{50}: >221 g a.i/ha**	No classification	
Aleochara bilineata	14-d laboratory (sand)	Select 240	**LR_{50}: >259 g a.i/ha**	No classification	
Chrysoperla carnea	6 weeks extended laboratory exposure to dry residues in conjunction with esterified rape seed oil (1.0 L/ha) on labortaory treated apple leaves	Select 240	**LR_{50}: >384 g a.i/ha**	No classification	
Birds					
Northern bobwhite quail, *Colinus virginianus*	Acute	Clethodim (82%)	LD_{50}: >2000 mg a.i./kg bw **LD_{50}: >1640 mg a.i./kg bw** (corrected for purity)	Practically non-toxic	1229456
	5-d Dietary	Clethodim (82%)	LC_{50}: >6000 mg a.i./kg diet; (LD_{50}: 637 mg a.i./kg bw/d)	Practically non-toxic	1229457
	22-w Reproduction	Clethodim (83.3%)	NOEC: 188 mg a.i./kg diet (reduced embryo viability) **(NOEL: 19.96 mg a.i./kg bw/d)**	No classification	1229460; 1229461
Mallard duck, *Anas platyrhynchos*	5-d Dietary	Clethodim (82%)	LC_{50}: >6000 mg a.i./kg diet **(LD_{50}: >339.4 mg** a.i./kg bw/d)	Practically non-toxic	1229459
	19-w Reproduction	Clethodim (83.3%)	NOEC: 833 mg a.i./kg diet (highest concentration tested) (NOEL: 47.12 mg a.i./kg bw/d)	No classification	1229462; 1229463

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Mammals					
Mice	Acute	Clethodim RE-45601 (83.3% purity)	LD_{50} (M) = 2570 mg/kg bw LD_{50} (♀) = 2430 mg/kg bw Signs: hypoactivity, rough coat, hunched posture, ataxia, urine stains, tremors, salivation Necropsy: in mice that died: slightly dark-red lungs, compound like material in the GI tract (no abnormalities noted in surviving mice)	Practically non-toxic	1229860-1
Rats		Clethodim RE-45601	LD_{50} (M) = 1630mg/kg bw LD_{50} (♀) = **1360 mg/kg bw** Signs: Day 1: salivation, ↓motor activity, clonic convulsions, tremoring and/or unsteady gait, hyperactivity, collapse. Day 2-6 in survivors: ↓food consumption, yellow anogenital staining. Necropsy: dark gelatinous material beneath the meninges, mottled/reddened lungs, foam in the trachea, very small lesions of gliosis in a single spinal nerve in lower lumbar area in 2 ♀'s at 1.45 g/kg bw.	Slightly toxic	1229862; 1232654
Rats		Imine sulfone RE-47719	LD_{50} (♀) > 1400 mg/kg bw	Slightly toxic	1227466
Rats		5-OH sulfone RE-51228 Vs. Clethodim RE-45601	5-OH sulfone LD_{50} (♀) > 1400 mg/kg bw (no mortality or clinical signs of toxicity, ↑bw of 63 g during the 14 day post-treatment period, no gross tissue	Slightly toxic	1227466

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			abnormalities) Clethodim Severe signs of toxicity (salivation, decreased motor activity, collapse, hyperactivity, tremors, ↓food consumption, diarrhoea, dehydration and nasal, ocular, oral and ano-genital discharges), all animals died within 3 days, ↓bw day 0-2, necropsy showed red discoloured lungs, blood pooled beneath the cranial meninges and black discoloured spleen, gastric mucosa, intestine and caecum		
Rats	2-generation Reproduction	Clethodim	Parental NOAEL: **20 mg /kg bw/d** (↓body weight, ↓food consumption (occasional) Offspring NOAEL: ≥140 mg /kg bw/d (↓pup body weight) [F_{1a}→F_{2a} generation, slight shaving lactation (0, -4.4%, -6.8%, -2.5%, -5.9% at day 0, 4, 7, 14, 21), but not stat. sig.] Reproduction NOAEL: ≥140 mg/kg bw/d (No treatment related effects observed in male and female mating, fertility and pregnancy rates; slight ↑incidence still born pups) (F_0 -> F_1 generation)* *Number of stillborn (%): F_{1a}->F_{2a} generation – 2 (0.7), 5(1.6), 5(1.7), 7(2.5), 14(5.8)	No classification	1227302-91, 1227399, 1234281

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Vascular plants					
Monocot crop species (onion, oat and corn); dicot crop species (rape, carrot and sunflower)	Tier I post emergence	Select 2 EC-01 (26.4% clethodim) + Para Sommer (75% paraffin oil) 1.2 v/v	Most sensitive monocot species was corn ER_{25}: 8 g a.i./ha NOEC: 4 g a.i./ha (Plant survival)	No classification	2416,2831
Dicot crop species (soybean, lettuce, carrot, tomato, cucumber and cabbage)	21d; 28-d Seedling emergence	Select (formulation containing 82.4% clethodim)	ER_{25}: >280 g a.i./ha NOEC: 280 g a.i./ha (highest dose tested)	No classification	1211499 2452940
Monocot crop species (onion, ryegrass, oat and corn)	Tier II 21-d Seedling emergence	Select (formulation containing 82.4% clethodim)	USEPA and study author's most sensitive species: oats Study author's endpoints: ER_{25}: 4.5 g a.i./ha ER_{50}: 51.8 g a.i./ha NOEC: 7.1 g a.i./ha (Plant height) USEPA's endpoints: ER_{25}: 8.5 g a.i./ha $ER_{25(NOEC)}$: 0.85 g a.i./ha (Plant height)	No classification	1211500 2452954 2452960
Oat (*Avena sativa*)		Select	ER_{50}: 54 g a.i./ha		2416,2864
Perennial ryegrass (*Lolium perenne*)		Select	ER_{50}: 0.7 g a.i./ha		
Corn (*Zea mays*)		Select	ER_{50}: 25 g a.i./ha		
Onion (*Allium cepa*)		Select	ER_{50}: > 280 g a.i./ha		
Dicot crop species (soybean, lettuce, carrot, tomato, cucumber and cabbage)	21d; 28-d vegetative vigour	Select (formulation containing 82.4% clethodim)	ER_{25}: >280 g a.i./ha NOEC: 280 g a.i./ha (highest dose tested)	No classification	1211497 2452940

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA ID
Monocot crop species (onion, ryegrass, oat and corn)	Tier II 21-d Vegetative vigour	Select (formulation containing 82.4% clethodim)	USEPA's most sensitive species: ryegrass Study author's endpoints: ER_{25}: 5.8 g a.i./ha ER_{50}: 6.7 g a.i./ha NOEC: 5.6 g a.i./ha (Plant dry weight) USEPA's endpoints ER_{25}: 5.8 g a.i./ha $ER_{25(NOEC)}$: 2.2 g a.i./ha (Plant dry weight) EAD's endpoints Most sensitive species: ryegrass ER_{25}: 6.97 g a.i./ha (plant height)	No classification	2455498 2455499 2455500 2416636
Ryegrass (*L. perenne*)		Clethodim	ER_{50}: 6.7 g a.i./ha	No classification	2416636
Cocksfoot grass (*D. glomerata*)		Clethodim	ER_{50}: 5.6 g a.i./ha		
Oat (*Avena sativa*)		Select	ER_{50}: 20 g a.i./ha		
Soybean (*Glycine max*)		Select	ER_{50}: >280 g a.i./ha		
Corn (*Zea mays*)		Select	ER_{50}: 17 g a.i./ha		
Onion (*Allium cepa*)		Select	ER_{50} > 280 g a.i./ha		
Lettuce (*Lactuca sativa*)		Select	ER_{50} > 280 g a.i./ha		
Carrot (*Daucus carota*)		Select	ER_{50} > 280 g a.i./ha		
Tomato (*Lycopersicon esculentum*)		Select	ER_{50} > 280 g a.i./ha **NOE_C: 2.89 g a.i./ha**		

[1] Adams *et al.* (1981) for bees and USEPA classification for others, where applicable

The avian dietary and reproduction endpoints were converted from concentration to daily dose using the following equation: Daily Dose = Concentration in food × (FIR/BW)
where: Concentration in food: Toxicity endpoint (for example, LC_{50} or NOEC), in mg a.i./kg diet
FIR: Food ingestion rate (equivalent to food consumption), in g diet/day
BW: Body weight, in g

Bold indicates most sensitive endpoints used in risk assessment

Table 9 Screening-level and refined risk assessment of clothianidin to beneficial arthropods

Organism	Exposure	Endpoint value	ESC	RQ (ESC/endpoint)	Is RQ > LOC? (LOC = 1 unless otherwise noted)	Implications for further refinements
Arthropods						
Aphidius rhopalosiphi (Parasitic wasp)	48 h, acute Laboratory test, 1:2 (v/v) mixture of Sulfoxaflor (25% chlorothalonil) and Pam Summer (75% Paraffin oil)	Exposure to residues on sprayed plants: LR_{50}: >240 g a.i./ha	In field – 93.2 g a.i./ha	<1.58	No	No refinement required. No unacceptable risk to parasitic wasps both on and off field
Typhlodromus cyani (Predatory mite)	168 h Extended laboratory test, leaf disks 1:2 (v/v) mixture of Sulfoxaflor (25% chlorothalonil) and Pam Summer (75% Paraffin oil)	LR_{50}: 7.6 g a.i./ha 75% corrected mortality (highest rate tested)	In field – 93.2 g a.i./ha	25.8	Yes (LOC <1 for extended & laboratory test)	Refinement required. Risks to predatory mites both on and off field at the highest and lowest application rates. No field studies available for refinement.
			off field (aerial application 25% of rates) – 20.979 g a.i./ha	7.63	Yes (LOC <1 for extended & laboratory test	
			off field (aerial application 6% of rates) – 5.07 g a.i./ha	1.72	Yes (LOC <1 for extended & laboratory test	
	168 h Extended laboratory test, leaf disks 1:2 (v/v) mixture of Sulfoxaflor (25% chlorothalonil) and Pam Summer (75% Paraffin oil)	LR_{50}: 7.6 g a.i./ha 75% corrected mortality (highest rate tested)	In field – 65.6 g a.i./ha	18.7	Yes (LOC <1 for extended & laboratory test)	
			off field (aerial application 25% of rates) – 16.40 g a.i./ha	4.68	Yes (LOC <1 for extended & laboratory test	

Organism	Exposure	Endpoint value	EEC	RQ (EEC/endpoint)	LOC exceeded? (LOC = 1 unless otherwise stated)	Implications for further refinements
			off field (aerial application 6% of rate) – 2.74 g a.i./ha	0.76	No	
Hesperhabra hellmeata	14-d laboratory (sand) Select 240	LR_{50} >259 g a.i./ha (0.115 mg/kg soil)	In field – 91.2 g a.i/ha (0.041 mg/kg soil)	<0.36	No	No refinement required. No unacceptable risk to ladybird beetle both on and off field
Chrysoperla carnea (green lacewing)	6 weeks extended laboratory exposure to dry residues in conjunction with esterified rape seed oil (1.0 L/ha) on laboratory treated apple leaves Select 240	LR_{50} >384 g a.i./ha	In field – 91.2 g a.i./ha	<0.24	No	No refinement required. No unacceptable risk to green lacewing both on and off field.
Poecilus cupreus	14-d laboratory (sand) 1:2 (v/v) mixtures of Select (25% clethodim/L.) and Para Sommer (75% Paraffin oil)	LR_{50} >256 g a.i./ha	In field – 91.2 g a.i/ha (0.041 mg/kg soil)	<0.42	No	No refinement required.
	14-d laboratory (sand) Select 240	LR_{50} >221 g a.i./ha	In field – 91.2 g a.i/ha (0.041 mg/kg soil)	<0.37	No	No refinement required.

Table 6 Screening level risk assessment of clethodim to earthworms, bees and terrestrial vascular plants

Organism	Exposure (Endpoint): Substance	Endpoint Value	EEC	RQ	Level of Concern Exceeded?
Invertebrates					
Earthworm (*Eisenia foetida*)	Acute Mortality (14-d LC_{50}/2): Clethodim	883.5 mg a.i./kg soil	0.041 mg a.i./kg soil[1]	0.0001	No
	Acute Mortality (14-d LC_{50}/2): Select	64.5 mg a.i./kg soil	0.041 mg a.i./kg soil[1]	0.0006	No
	Acute Mortality (14-d LC_{50}/2): Clethodim 240	42.45 mg a.i./kg soil	0.041 mg a.i./kg soil[1]	0.0010	No
	Acute Mortality (14-d LC_{50}/2): Clethodim sulfoxide	>500 mg a.i./kg soil	0.042 mg a.i./kg soil[1]	<0.0001	No
Bees (*Apis mellifera*)	Acute Contact (48-h LC_{50}): Clethodim	37.29 µg a.i./bee	2.64 µg a.i./bee[1]	0.071	No
	Acute Contact (48-h LD_{50}): Select 2.0	>33 µg a.i./bee	2.64 µg a.i./bee[1]	<0.08	No
	Acute Oral (48-h LD_{50}): clethodim	313 µg a.i./bee	0.219 µg a.i./bee[2]	0.0007	No
	Acute Oral (48-h LD_{50}): Select 240	>43 µg a.i./bee	0.219 µg a.i./bee[2]	<0.005	No
Vascular plants					
Ryegrass, Cockspur grass, soybean, corn, onion, lettuce, carrot and Tomato	Species Sensitivity Distribution (HC_5): Vegetative vigour	2.39 g a.i./ha	91.2 g a.i./ha	**35.16**	Yes (LOC >1 at the screening level)
		2.39 g a.i./ha	45.6 g a.i./ha	**19.08**	Yes (LOC >1 at the screening level)

[1] Endpoint derived according to Koch and Weißer (1997), whereby the proposed upper-bound residue value for estimating exposure to bees is based on a maximum residue value: 0.0912 kg a.i./ha × 2.4 µg a.i./bee per kg/ha = 0.219 µg a.i./bee.

[2] Endpoint based on consumption rates primarily derived from Rortais et al. (2005) and Crailsheim et al. (1992 and 1993), whereby the oral exposure estimate for adult bees is calculated by multiplying the direct single rate by 29 µg a.i./bee per kg/ha: 0.0912 kg a.i./ha × 29 µg a.i./bee per kg/ha = 2.645 µg a.i./bee.

Table 7 Estimated Environmental Concentrations (EEC) in vegetation and insects

Food item	EEC (mg a.i./kg fw)[a]		Fresh / dry weight ratios	EEC (mg a.i./kg dw)	
	Maximum Residues	Mean Residues		Maximum Residues	Mean Residues
Short range grass	20	7	3.3[b]	64	23
Leaves and leafy crops	11	4	11[b]	121	40
Long grass	9	3	4.4[b]	39	13
Forage crops	11	4	5.4[b]	60	20
Small insects	5	3	3.8[c]	18	10
Pods with seeds	1.2	0.6	3.9[c]	5	2.2
Large insects	1.2	0.6	3.8[c]	5	2.2

Grain and seeds	1.2	0.6	3.8[c]	5	2.2
Fruit	1.2	0.6	7.6[c]	9	4.3

[a] Based on correlations reported in Hoerger and Kenaga (1972) and Kenaga (1973) and modified by Fletcher (1994)
[b] Fresh / dry weight ratios from Harris (1975)
[c] Fresh / dry weight ratios from Spector (1956)

Table 8 Further characterization of risk to Terrestrial Vascular Plants

Species	Endpoint	On-field		Aerial Application (23% spray drift)		Ground Application (6% spray drift)	
				Off Field		Off-field	
		EEC (g a.i./ha)	RQ	EEC (g a.i./ha)	RQ	EEC (g a.i./ha)	RQ
Ryegrass, Cockspur grass, soybean, corn, onion, lettuce, carrot and Tomato	Species Sensitivity Distribution (HC_5): 2.39 g a.i./ha	91.2	**38.16**	20.98	**8.8**	5.472	**2.3**
		45.6	**19.08**	10.5	**4.4**	2.736	**1.14**

Bold cells indicate that the level of concern is exceeded (LOC = 1).

Table 9 Screening level risk assessment of clethodim to birds and mammals

	Toxicity (mg ai/kg bw/d)	Feeding Guild (food item)	EDE (mg ai/kg bw/d)	RQ
Small Bird (0.02 kg)				
Acute	164	Insectivore (insects)	4.60	0.028
Reproduction	19.96	Insectivore (insects)	4.60	0.23
Medium Sized Bird (0.1 kg)				
Acute	164	Insectivore (insects)	3.59	0.022
Reproduction	19.96	Insectivore (insects)	3.59	0.18
Large Sized Bird (1 kg)				
Acute	164	Herbivore (short grass)	3.74	0.023
Reproduction	19.96	Herbivore (short grass)	3.74	0.19
Small Mammal (0.015 kg)				
Acute	136	Insectivore (insects)	2.64	0.019
Reproduction	28	Insectivore (insects)	2.64	0.09
Medium Sized Mammal (0.035 kg)				
Acute	136	Herbivore (short grass)	8.28	0.061
Reproduction	28	Herbivore (short grass)	8.28	0.30
Large Sized Mammal (1 kg)				
Acute	136	Herbivore (short grass)	4.42	0.033
Reproduction	28	Herbivore (short grass)	4.42	0.16

[a] Food Ingestion Rates (Nagy, 1987). For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; for generic birds with body weight greater than 200 g, the

	Toxicity (mg ai/kg bw/d)	Feeding Guild (food item)	EDE (mg ai/kg bw/d)	RQ
"all birds" equation was used: Passerine Equation (body weight < or =200 g): FIR (g dry weight/day) = 0.398(BW in g)$^{0.850}$ All birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648(BW in g)$^{0.651}$. For mammals, the "all mammals" equation was used: FIR (g dry weight/day) = 0.235(BW in g)$^{0.822}$ [b] EDE = Estimated dietary exposure; is calculated using the following formula: (FIR/BW) × EEC. At the screening level, food items representing the most conservative EEC for each size guild are used. Shaded cells indicate that the level of concern is exceeded (LOC = 1).				

Table 10 Toxicity of clethodim and end-use products to Non-Target aquatic Species

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Freshwater species					
Daphnia magna	48-h Acute	Clethodim Agan TGAI (95.8% purity)	EC_{50}: **101.64 mg a.i./L**	Practically non-toxic	1074750
	48-h Acute	Select 240 EC Formulation (240 g/L)	EC_{50}: 22.06 mg form./L Equivalent to EC_{50}: 5.3 mg a.i./L	Moderately toxic	1074722
	48-h Acute	Select 2EC formulation (25.6%)	EC_{50}: 20.2. mg form./L Equivalent to **EC_{50}: 5.1 mg a.i./L**	Moderately toxic	2416283/ 2416285
	48-h Acute	Select 240 EC formulation (240 g clethodim/L)	EC_{50}: 21 mg form./L Equivalent to EC_{50}: 5.2 mg a.i./L	Moderately toxic	2416283
	21-d Chronic	clethodim (92.4% purity)	NOEC: 49 mg a.i./L (parental survival and reproduction)	No classification	2416283
	21-d Chronic	Select(25.6%) + oily adjuvant	**NOEC: 0.00084 mg a.i./L**	No classification	2416284
	21-d Chronic	TM-20016 (240 g/L clethodim formulation without oily adjuvant)	NOEC: 0.51 mg a.i./L (nominal concentration)	No classification	
	21-d Chronic	Clethodim Agan TGAI (95.8% purity)	**NOEC: 0.94 mg a.i./L** LOAEC: 3.0 mg a.i./L	No classification	2452948

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Sediment dwelling invertebrate, *Chironomus riparius*	28-d Chronic, spiked water	Clethodim imine (chemical purity 97.6%)	**NOEC: 10 mg a.i./L** (total emergence) nominal concentration	No classification	2416283
Rainbow trout, *Oncorhynchus mykiss*	96-h Acute	Clethodim technical (RE-45601) (83.3%)	**LC_{50}: 24.4 mg a.i./L**	Slightly toxic	1227450
	96-h Acute	Clethodim technical (95.4%)	LC_{50}: >110 mg a.i./L	Practically non-toxic	2416285
	96-h Acute	Select 240 EC (25.5% w/w clethodim)	LC_{50}: 13 mg formulation./L **(3.4 mg a.i./L)**	Moderately toxic	2416283
	96-h Acute	Clethodim sulfoxide	**LC_{50}: >100 mg a.i./L** (mortality, nominal concentrations)	Practically non-toxic	2416284
	21-d prolonged toxicity study	Clethodim (95.2%)	NOEC: 3.9 mg/L (mean measured concentration)	No classification	2416283
	21-d prolonged toxicity study	Select(25.6%) + oily adjuvant	**NOEC: 0.29 mg/L** (mean measured concentration)	No classification	2416284
	21-d prolonged toxicity study	TM-20016 (240 g/L clethodim formulation without oily adjuvant	NOEC: 1.1 mg/L (nominal concentrations)	No classification	
Bluegill sunfish *Lepomis macrochirus*	96-h Acute	Clethodim technical (RE-45601) (83.3%)	LC_{50}: >33 mg a.i./L	Slightly toxic	1229464
Zebra fish *Danio rerio*	96-h Acute	Clethodim Agan technical (97.5%)	LC_{50}: 134.2 mg/L	Practically non-toxic	1074751
	96-h Acute	Clethodim 240 g/L CE formulation	LC_{50}: 24 mg formulation./L (5.8 mg a.i./L)	Moderately toxic	1074730
Fathead minnow, *Pimephales promelas*	96-h Acute	Clethodim technical (95.4%)	LC_{50}: 110 mg a.i./L	Practically non-toxic	2416285
	Early-life stage	Clethodim technical (95.7%)	**NOEC: 0.010 mg a.i./L** (survival) LOEC: 0.031 mg a.i./L	No classification	2452948
Green algae, *Pseudokirchneriella subcapitata*	120-h Acute	Clethodim (83.3%)	EC_{50}: >11.4 mg a.i./L (measured concentration)	No classification	1234998; 1234999

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
	72-h Acute	Clethodim Agan Technical (97.5%)	**EC_{bs0}: 3.87 mg /L** (biomass)	No classification	1074757
	72-h Acute	Clethodim 240g/L CE formulation	EC_{50}: 33.55 mg clethodim 240g/L (approximately 8.1 mg a.i./L of each active ingredient) (cell density/biomass)	No classification	1074732
	72-h Acute	Select 2.0 EC (25.6%)	Most sensitive endpoint: EC_{50}: 4.6 mg a.i./L (biomass)	No classification	2416283
Green alga, *Scenedesmus subspicatus*	72-h Acute	Clethodim (92.4%)	Most sensitive endpoint: EC_{50}: 36 mg/L (biomass)	No classification	2416283
	72-h Acute	Select 2.0 EC (26..6%) formulation containingPara Sommer1:2v/v)	Most sensitive endpoint: **EC_{50}: 1.5 mg a.i./L** (biomass)	No classification	2416283
Green alga, *Desmodesmus subspicatus*	72-h Acute	Clethodim sulfoxide (99.4%)	**EC_{50}: >100 mg/L** (biomass)	No classification	2416283
Green alga, *Chlorella vulgaris*	96-h- Acute	Clethodim EC (12%)	EC_{50}: 4.6 mg a.i./L (growth rate)	No classification	2416285
Green alga, *Raphidocelis subcapitata*	96-h- Acute	Clethodim EC (12%)	EC_{50}: 2.7 mg a.i./L (growth rate)	No classification	2416285
Blue-green algae, *Anabaena flos-aquae*	72-h Acute	Select 2.0 EC (25.6%.)	Most sensitive endpoint: **EC_{50}: 3.2 mg a.i./L** (growth rate)	No classification	2416283
Diatom, *Navicula pelliculosa*	96-h Acute	Clethodim (94.8%)	EC_{50}: 36 mg/L (biomass) EC_{50}: 56 mg/L (growth rate)	No classification	2416283
	72-h Acute	Select 2.0 EC (25.6%.)	Most sensitive endpoint: EC_{50}: 5.4 mg a.i./L (biomass)	No classification	2416283

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Monocot vascular plant, duckweed, *Lemna gibba*	7-d Semi static	Clethodim Technical (94.2%)	Most sensitive endpoint: **EC_{50}: 5.8 mg a.i./L** (frond area)	No classification	1371484
	14-d Static	RE-45601 technical (82.4%.)	Most sensitive endpoint: **EC_{50}:1.34 mg a.i../L** (frond counts)	No classification	2416283; 2452948
	14-d Static	Clethodim technical (91.1%.)	Most sensitive endpoint: EC_{50}: > 4. 8 mg a.i./L (growth rate)	No classification	2416283
	14-d Semi-Static	Select 2.0 EC (25.6%.)	Most sensitive endpoint: **EC_{50}: 42.5. mg a.i./L** (frond counts)	No classification	2416283; 2452948
Marine/estuarine species					
Eastern Oyster, *Crassostrea virginica*	96-h Acute	clethodim Technical (95.4%.)	**96-hr EC_{50} = 5.3 mg a.i./L**	moderately toxic	2452948 2452961 2452951
Saltwater mysids *Americamysis bahia*	96-h Acute	clethodim Technical (95.4%.)	**96-hr EC_{50} = 33 mg a.i./L**	slightly toxic	2452949 2452948 2452961
Sheepshead minnow, *Cyprinodon variegatus*	chronic	clethodim Technical (95.4%.)	NOEC: 4.2 mg a.i./L	No classification	2452950 2452948 2452961
Marine diatom, *Skeletonema costatum*	EFSA 72-h Acute	Select 2.0 EC (25.6%)	Most sensitive endpoint: **EC_{50}: 5.3 mg a.i./L** (biomass)	No classification	2416283
	EPA 120-h Acute		Most sensitive endpoint: EC_{50}: 8.6 mg/L (biomass)	No classification	2416285

[1] USEPA classification, where applicable; **Bold** indicate most sensitive endpoints used in risk assessment.
TGAI = technical grade active ingredient

Table 11 Screening level risk assessment of clethodim and transformation products for aquatic organisms

Organism	Exposure (Endpoint): Substance	Endpoint Value (mg a.i./L)	EEC	RQ	Level of Concern Exceeded?
Freshwater species					
Daphnia magna	Acute (48-h EC_{50}/2): Clethodim	50.82	0.0114	0.0002	No
	Acute (48-h EC_{50}/2): Select 2 EC (25.6%)	2.55	0.0114	0.0045	No
	Chronic (21-day NOEC): Clethodim	0.94	0.0114	0.0121	No

	Chronic (21-day NOEC): Select + Oily adjuvant	0.00084	0.0114	**13.57**	Yes
Benthic Invertebrate (chironomid)	Chronic (28-day NOEC): Clethodim imine	10	0.009	0.0009	No
Rainbow Trout	Acute (96-h LC_{50}/10): Clethodim	2.44	0.0114	0.005	No
	Acute (96-h LC_{50}/10): Select 240 EC	0.34	0.0114	0.034	No
	21-d prolonged NOEC: Select 25.6%	0.29	0.0114	0.039	No
	Acute (96-h LC_{50}/10): Clethodim sulfoxide	>10	0.012	<0.001	No
Fathead Minnow	Chronic (32-d early - life cycle NOEC): Clethodim	0.01	0.0114	**1.14**	Yes
Amphibians (most sensitive fish)	Acute (96-h LC_{50}/10): Select 240 EC	0.34	0.061	0.18	No
	Chronic (early-life cycle NOEC): clethodim	0.01	0.061	**6.10**	Yes
Freshwater alga (green - *Pseudokirchneriella subcapitata*)	Acute (72-h EC_{50}/2): Clethodim	1.94	0.0114	0.006	No
Scenedesmus subspicatus	Acute (72-h EC_{50}/2): Select + Para Sommer	0.75	0.0114	0.015	No
Anabaena flos-aquae	Acute (72-h EC_{50}/2): Select 2.0 EC	1.6	0.0114	0.007	No
Desmodesmus subspicatus	Acute (72-h EC_{50}/2): Clethhodim sulfoxide	>10	0.012	<0.0002	No
Vascular plant (duckweed - *Lemna gibba*)	Acute (7-day EC_{50}/2): Clethodim	2.9	0.0114	0.004	No
	Acute (14-day EC_{50}/2): Clethodim	0.67	0.0114	0.017	No
	Acute (14-day EC_{50}/2): Select 2.0 EC	21.25	0.0114	0.0005	No
Marine Species					
Saltwater mysids *Americamysis bahia*	Acute (96-h EC_{50}/2): Clethodim	16.5	0.0114	0.0007	No
Eastern Oyster, *Crassostrea virginica*	Acute (96-h EC_{50}/2): Clethodim	2.65	0.0114	0.004	No
Marine algae (diatom- (*Skeletonema costatum*)	Acute (72-h EC_{50}/2): Select 25.6%	2.65	0.0114	0.004	No

Sheepshead minnow, *Cyprinodon variegatus*	Chronic (34-d early-life cycle NOEC): Clethodim	4.2	0.0114	0.003	No

Table 12 Risk Quotients for aquatic organisms determined for drift of clethodim

Organism	Exposure	Endpoint value	Refined EEC	RQ	Level of Concern
Freshwater invertebrate (*Daphnia magna*)	Water-sediment system	NOEC = 0.00084 mg a.i./L	Aerial appl. (23% drift): 0.0026 mg a.i./L	3.1	**Exceeded**
			Ground appl. (6% drift): 0.0007 mg a.i./L	0.8	Not exceeded
Freshwater fish – rainbow trout	Water-sediment system	NOEC = 0.01 mg a.i./L	Aerial appl. (23% drift): 0.0026 mg a.i./L	0.3	Not exceeded
			Ground appl. (6% drift): 0.0007 mg a.i./L	0.1	Not exceeded
Amphibia (*Xenopus laevis*)	Water-sediment system	NOEC = 0.01 mg a.i./L	Aerial appl. (23% drift): 0.01403 mg a.i./L	1.4	**Exceeded (marginally)**
			Ground appl. (6% drift): 0.0037 mg a.i./L	0.4	Not exceeded
Level of concern exceeded for values in **bold** (RQ > 1)					

Table 13 Risk Quotients for Aquatic Organisms Determined for Runoff of clethodim in Water Bodies 80 or 15 cm deep

Organism (exposure)	Endpoint value	EEC concentrations (time-frame, water body)	RQ	Level of Concern
Freshwater Fish (Chronic risk)	NOEC: 0.01 mg a.i./L	90 day, 80 cm water body: 0.0014mg a.i./L	0.14	Not exceeded
Amphibians (Chronic risk)	NOEC: 0.01 mg a.i./L	90 day, 15 cm water body: 0.0043mg a.i./L	0.43	Not exceeded
Level of concern exceeded for values in **bold** (RQ > 1)				

Appendix IX Proposed Label Amendments for Products Containing Clethodim

The label amendments presented below are proposed for technical and end-use products, as applicable. These label amendments do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Information on labels of currently registered products should not be removed unless it contradicts the label statements below.

Use Precautions:

Replace:

- "When handling the concentrate, mixing, loading or during cleanup and repair, wear goggles or face shield, rubber apron, chemically resistant gloves, rubber boots, long sleeved shirt and long legged pants."

With:

- "When handling the concentrate, mixing, loading or during cleanup and repair, wear goggles or face shield, rubber apron, chemically resistant gloves, rubber boots, long sleeved shirt and long legged pants. Wear long sleeved shirt, long legged pants and chemical-resistant gloves during spraying application. Chemical resistant gloves are not required to be worn during groundboom or aerial application."

Add

- "Apply only when the potential for drift to areas of human habitation or areas of human activity such as houses, cottages, schools and recreational areas is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings."

Directions for Use

Add

- Not for use in greenhouses.
- 1 year plant back interval for all non-registered food and feed crops.

Environmental Hazards:

Add:

TOXIC to aquatic organisms and non-target terrestrial plants.

Observe buffer zones specified under DIRECTIONS FOR USE.

Toxic to certain beneficial insects. Minimize spray drift to reduce harmful effects on beneficial insects in habitats next to the application site such as hedgerows and woodland.

To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay.

Avoid application when heavy rain is forecast.

Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.

This product contains aromatic petroleum distillates that are toxic to aquatic organisms.

The use of this chemical may result in contamination of groundwater particularly in areas where soils are permeable (for example, sandy soil) and/or the depth to the water table is shallow.

Replace:

"Avoid spray drift. Avoid contamination of ponds, streams, rivers and desirable vegetation".

OR

"Avoid contamination of aquatic systems during application. Do not contaminate these systems through direct application, disposal of waste or cleaning equipment"

With:

As this product is not registered for the control of pests in aquatic systems, DO NOT use to control aquatic pests.

DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

Storage:

Replace:
May be stored at any temperature. SHAKE WELL BEFORE USING. Insecticides and fungicides should be segregated from herbicides so as to prevent the possibility of cross contamination.

With:

To prevent contamination, store this product away from food or feed.

Buffer Zone Related Label Statements:

For products registered for aerial and field sprayer application, add:

Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572.1) medium classification. Boom height must be 61 cm or less above the crop or ground.

Aerial application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply when wind speed is greater than 16 km/h at flying height at the site of application. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572.1) medium classification. To reduce drift caused by turbulent wingtip vortices, the nozzle distribution along the spray boom length **MUST NOT** exceed 75% of the wing or rotorspan.

Buffer zones:

Use of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer and spot treatment.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, riparian areas and shrublands) and sensitive freshwater habitats (such as lakes, rivers, sloughs, prairie potholes, creeks, marshes, streams, reservoirs and wetlands).

Buffer Zone Table for products registered for aerial and field sprayer application:

Method of application	Crop	Buffer Zones (metres) Required for the Protection of:		
		Freshwater Habitat of Depths:		Terrestrial habitat
		Less than 1 m	Greater than 1 m	
Field sprayer	Seedling stalk, without bladders, cauliflower, coriander (cilantro), dry onion, elephant garlic, fava bean, fennel, garlic, ground brown mustard (condiment and oilseed types), yellow mustard, peas, soybean, sunflower	1	1	3

	Speed, for common turf, flea and tick pest control		1	1	1
weed	Grass, for field and pasture, prairie, rights-of-way, timber, uncultivated areas, wastelands	Ground spray	10	1	60
		Aerial spray	10	1	60
	For common turf, flea and tick pest control	Ground spray	8	1	40
		Aerial spray	1	1	40

For tank mixes, consult the labels of the tank mix partners and observe the largest cross contamination buffer zone of the products involved in the tank mixtures and apply using the coarse spray (VMD) category indicated on the labels for those tank mix partners.

The buffer zones for this product can be modified based on weather conditions and spray equipment configuration by accessing the Buffer Zone Calculator on the Pest Management Regulatory Agency web site.

For products registered for field sprayer application only, add:

Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572) medium classification. Boom height must be 60 cm or less above the crop or ground.

DO NOT apply by air.

Buffer zones:

Use of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer and pet treatment.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, riparian areas and shrublands) and sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands).

Method of application	Crop	Buffer Zones (metres) Required for the Protection of:		
		Freshwater Habitat of Depths:		Terrestrial habitat
		Less than 1 m	Greater than 1 m	
Field sprayer	Seedling alfalfa, highbush blueberry, cranberry, coriander, fenugreek, dry onion, safflower, canola, flax, field pea, lentils, oriental (brown) mustard (condiment and oilseed types), yellow mustard, potato, soybean, sunflower,	1	1	2
	Spinach, dry common bean, Desi and Kabuli chickpea, Prairie coriander	1	1	1

For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners.

The buffer zones for this product can be modified based on weather conditions and spray equipment configuration by accessing the Buffer Zone Calculator on the Pest Management Regulatory Agency web site.

References

A. Information Considered in the Chemistry Assessment

List of Studies/Information Submitted by the Registrant

PMRA Document Number	Reference
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2079982	2010, Cletodim Tecnico : Density, DACO: 2.14.6
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2215011	2012, Clethodim Technical: Description of Manufacturing Process, DACO: 2.0, 2.1, 2.11, 2.11.2, 2.11.3, 2.11.4, 2.12, 2.12.1, 2.13, 2.13.1, 2.13.2, 2.13.3, 2.13.4, 2.14, 2.2, 2.3, 2.3.1, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9
2262172	2009, AMENDED ANALYTICAL REPORT Batch Analysis of Clethodim and Impurities, DACO: 3.0,3.1,3.3.1,3.4
2215009	2012, Clethodim: Product Chemistry Analysis, DACO: 2.0,2.12.1,2.13,2.13.2
2262172	2009, AMENDED ANALYTICAL REPORT Batch Analysis of Clethodim and Impurities, DACO: 3.0,3.1,3.3.1,3.4
2215009	2012, Clethodim: Product Chemistry Analysis, DACO: 2.0,2.12.1,2.13,2.13.2
637505	2003, Physical State, Shape, Colour And Odour Of Clethodim Agan Technical., DACO: 2.14.1,2.14.2,2.14.3
637508	2003, Determination Of The Density Of Clethodim Agan Technical., DACO: 2.14.6
637511	2003, Solubility Of Clethodim Agan Technical In Water And Organic Solvents., DACO: 2.14.7,2.14.8
637512	2003, Vapour Pressure Of Clethodim Agan Technical., DACO: 2.14.9
637513	2003, Dissociation Constants In Water Of Clethodim Agan Technical. B, DACO: 2.14.10
637514	2003, Partition Coefficient (N-Octanol/Water) Of Clethodim Agan Technical., DACO: 2.14.11
637515	2003, UV/VIS Absorption Spectra Of Clethodim Agan Technical., DACO: 2.14.12
637509	2003, Thermal And Air Stability Of Clethodim Agan Technical., DACO: 2.14.13
637502	2003, Description Of Starting Material.; Detailed Production Process Description; Discussion of Formation of Impurities, DACO: 2.11.2,2.11.3,2.11.4
637503	2003, Clethodim Technical Five Lots Analysis And Method Validation., DACO: 2.13.1,2.13.3
1292788	2006, Clethodim Technical - 5-Lots Analysis and Method Validation, DACO: 2.13.1,2.13.2,2.13.3
637503	2003, Clethodim Technical Five Lots Analysis And Method Validation., DACO: 2.13.1,2.13.3
1292788	2006, Clethodim Technical - 5-Lots Analysis and Method Validation, DACO: 2.13.1,2.13.2,2.13.3

B. Information Considered in the Toxicological Assessment

List of Studies/Information Submitted by Registrant

PMRA Document Number	Reference
1226179 and 1232645	1986, Microbial/mammalian microsome mutagenicity plate incorporation assay with RE-45601 technical (83.3% purity, SX-1688) (CEHC 2555), DACO: 4.5.4
1226180, 1226185-88, 1226982, 1231837 and 1234279	1988, Chronic oral oncogenicity study in mice with Chevron RE-45601 technical (SX-1688)(2107-145), DACO: 4.4.2
1226181 and 1232646	1986, Microbial/mammalian microsome mutagenicity plate incorporation assay with RE-45601 (83% purity, SX-1688)(SOCAL 2505), DACO 4.5.4
1226182 and 1232647	1986, Chromosome aberrations in Chinese hamster ovary (CHO) cells with Chevron RE-45601 technical (T4529.337), DACO: 4.5.4
1226183 and 1232643	1987, Cytogenetics assay in bone marrow cells of rats following acute oral exposure to RE-45601 technical (T5072.105), DACO: 4.5.4
1226184 and 1232648	1986, In vivo-in vitro hepatocyte DNA repair assay: in vitro evaluation of unscheduled DNA synthesis (UDS) following oral administration of Chevron RE-45601 technical to B6C3F1 mice (LSC-1960), DACO: 4.5.4
1227357	1988, Five week oral toxicity study in rats with RE-47719 (SX-1800)(CEHC 2949), DACO: 4.6.1
1227358	1988, Five week oral toxicity study in rats with RE-51228 (SX-1803). (CEHC 2950), DACO: 4.3.1
1227359	1988, Oral teratogenicity and developmental toxicity screen in rats with RE-47719 (303-012), DACO: 4.5.2
1227360	1988, Oral teratogenicity and developmental toxicity screen in rats with RE-51228 (303-010), DACO: 4.5.2
1227361	1988, Microbial/mammalian microsome plate incorporation mutagenicity assay with RE-47719 (SX-1800) (CEHC 2948), DACO: 4.5.4
1227362	1988, Chromosome aberrations in Chinese hamster ovary (CHO) cells: RE-47719 – Final toxicity report (TR226.337003), DACO: 4.5.4
1227371-77, 1227379, 1227381, 1227451, 1227453-59, 1230580 and 1230582-85	1988, Combined chronic oral toxicity/oncogenicity study in rats with RE- 45601 technical (SX-1688) (SOCAL 2500), DACO: 4.4.1, 4.4.2.
1227382-91, 1227399 and 1234281	1987, Two generation (one litter) reproduction study in rats with RE-45601 technical (CEHC 2596), DACO: 4.5.1
1227466	1988, The comparative acute oral toxicity of RE-47719 (SX-1800) and RE-45601 technical (SX-1688) in adult female rats (2952), DACO: 4.2.1
1227467	1988, The comparative acute oral toxicity of RE-51228 (SX-1796) and RE-45601 technical (SX-1688) in adult female rats (2951), DACO: 4.2.1
1227481	1987, Four-week repeated-dose dermal toxicity study in rats with RE-45601 technical (SX-1688) (CEHC 2552), DACO: 4.3.4

PMRA Document Number	Reference
1228811, 1228823, 1231978-79 and 1234282	1987, Teratology study in rats with Chevron RE-45601 technical (86-3042), DACO: 4.5.2
1228837, 1228848 and 1228859	1987, Teratology study in rabbits with Chevron RE-45601 (303-007), DACO: 4.5.2
1229446	1987, Microbial/mammalian microsome plate incorporation mutagenicity assay with RE-51228 (CEHC 2856), DACO 4.5.4
1229458	1988, Chromosome aberrations in Chinese hamster ovary (CHO) cells: RE-51228 (T8227.337003), DACO: 4.5.4
1229860-61	1986, Acute oral toxicity study in mice with Chevron RE-45601 technical (SX-1688)(2107-143), DACO: 4.2.1
1229862 and 1232654	1986, The acute oral toxicity of RE-45601 technical. (SX-1688) in adult male and female rats (SOCAL 2498), DACO: 4.2.1
1229863 and 1232667	1986, The acute dermal toxicity of RE-45601 technical (SX-1688) in adult male and female rabbits (CEHC 2510), DACO: 4.2.2
1229864 and 1232669	1986, The acute inhalation toxicity of RE-45601 technical (SX-1688) in rats (CEHC 2513), DACO: 4.2.3
1229865 and 1232670	1986, The acute eye irritation potential of RE-45601 technical (SX-1688) (CEHC 2511), DACO: 4.2.4
1229866 and 1232671	1986, The four-hour skin irritation potential of RE-45601 technical (SX-1688) (CEHC 2512), DACO: 4.2.5
1229868 and 1232673	1986, Modified Buehler test for the skin sensitization potential of RE-45601 technical (SX-1688) (CEHC 2514), DACO: 4.2.6
1229869, 1231831 and 1231977	1986, Four-week subchronic oral toxicity study in mice with RE-45601 technical (SX-1688) (2107-140), DACO: 4.3.1
1229870-71	1986, Five week pilot feeding study in rats with RE-45601 technical (SX-1653) (SOCAL 2457), DACO: 4.3.1
1229872-74, 1229882 and 1232674	1986, 13-week oral toxicity study in rats with RE-45601 technical (SX-1688) (SOCAL 2501), DACO: 4.3.1
1229893 and 1231833	1987, A ninety-day subchronic oral toxicity study in dogs with Chevron RE-45601 technical (85-2999), DACO: 4.3.1
1229901	1988, One-year oral toxicity study in dogs with Chevron RE-45601 technical (SX-1688) (2107-153), DACO: 4.3.1
1227015 and 1232651	1988, The in vivo metabolism of [Propyl-1-^{14}C] clethodim in rats (2515) (721.14), DACO: 6.4
1371485-86	2006, Clethodim technical: acute oral neurotoxicity (gavage) study in rats (A76937), DACO: 4.5.12
2308444	2012, A 90-day oral dietary neurotoxicity study of clethodim in rats (194040) (38046), DACO: 4.5.13
2308446	2012, A 28-day dietary dose range-finding neurotoxicity study of clethodim in rats (194039) (38041), DACO: 4.5
2308448	2012, A 28-day oral (dietary) range-finding immunotoxicity study of clethodim in female B6C3F1 mice (194037) (37831), DACO: 4.8(B)
2308450	2012, A 28-day oral (dietary) immunotoxicity study of clethodim in female B6C3F1 mice (194038) (37839), DACO: 4.8(B)

Additional Information Considered

i) Published Information

PMRA Document Number	Reference
2456234	2007, Clethodim: Human Health Risk Assessment for Proposed Uses on Herb Subgroup 19A, Leafy Greens Subgroup 4A, Sesame seed, Safflower seed, Legume Vegetable Group 6, Hops, Asparagus, and Flax seed. USEPA Memorandum. PC Code: 121011, Petition Nos.: 4E6836, 5E6978, 4F6895, 5E6977, and 3E6555. DP Number: D323144, March 7, 2007
2456235	2008, Revised Clethodim Human Health Assessment Scoping Document in Support of Registration Review. USEPA Memorandum. PC Code: 121011, DP Number : D356151 & D349757, September 9, 2008
2456236	2014, Clethodim. Preliminary Risk Assessment for Registration Review. USEPA Memorandum. PC Code: 121011, DP Number : D356151 & D349757, January 30, 2014
2456233	1993, Clethodim. Summary of Toxicology Data. California EPA. November 9, 1993

C. Information Considered in the Occupational and Non-Occupational Assessment

Registrant Submitted Studies/Information

PMRA Document Number	Reference
1227004	THE PERCUTANEOUS ABSORPTION OF 14C - SELECT 2,0 EC (RE-45601) IN MALE RATS (2774), DACO: 6.4
1143600	HERBICIDES: CLETHODIM: SELECT: A STUDY TO DETERMINE THE EXPOSURE OF HERBICIDE APPLICATIORS TO CLETHODIM FROM MIXING AND APPLYING SELECT (444-90PT;90-P1197;C080983;90-167PT), DACO: 5.1
2115788	Agricultural Reentry Task Forces (ARTF). 2008. Data Submitted by the ARTF to Support Revision of Agricultural Transfer Coefficients.

Additional Information Considered

i) Published Information
None

ii) Unpublished Information

PMRA Document Number	Reference
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2381029	DACO: 5.4_Review

D. Information Considered in the Dietary Assessment

Registrant Submitted Studies/Information

PMRA Document Number	Reference
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1058015	2005. Clethodim: Magnitude of the Residue on Coriander. AAFC Study # AAFC03-046, pages 1-119 of 213 pages. GLP. Unpublished.
1065760	1993. Confirmatory Method for the Determination of Clethodim and Clethodim Metabolites in Crops, Animal Tissues, Milk, and Eggs, Method: EPA-RM-26D-2.
1065761	1994. PR Notice 88-5 Validation of Valents Confirmatory Method for the Determination of Clethodim and Clethodim Metabolites in Crops, Animal Tissues, Milk, and Eggs: Method EPA-RM-26D-2 (Revision February 1, 1993)
1065764	1990b. Freezer Storage Stability of Clethodim Residues on Cottonseed Processed Parts.
1065765	1991. Freezer Storage Stability of Clethodim Residues on Soybean Processed Parts.
1065766	1988. Confined Rotational Crop Study of [Ring-4, 6-14C] Clethodim with Carrots, Lettuce and Wheat. Chevron Chemical Company, Laboratory Project Identification MEF-0036, 99 Pg.
1148244	1992. Herbicides: Clethodim: Select Residue Studies in Potatoes,Canada,1990-1991 (REF:92-001.DC)
1148245	1992. Herbicides: Clethodim: Select Residue Studies in Soybeans,Canada,1990-1991 (REF:92-002.DC)
1157287	1995. Herbicides: Clethodim: Select Residue Studies in Lentils Canada 1993-1994; REF: 94-102.DC (January 1995)
1160760	1995. Herbicides: Clethodim: Select: Residue Studies in Alfalfa, Canada, 1993-1994.(REF:95-040.DC)
1160766	1995. Herbicides: Clethodim: Select: Residue Studies in Peas, Canada, 1993-1994.(REF:95-036.DC).
1171065	1996. Herbicides: Clethodim: Select. Residue Studies in Mustard, Canada, 1994-1995. April 1996. (REF:96-034.DC)
1171066	1996. Herbicides: Clethodim: Select. Residue Studies in Sunflower/Sunola, Canada, 1994-1995. April 1996. (REF:96-035.DC)
1175023	1998. Magnitude of Residues in Processed Sunflower Seed. Analytical Portions of the Processing Study for Argentina. Date Stamped-"Received Health Evaluation Division Mar 5 1998".(TMN-765;M-387;T-701).(Clethodim)
1175024	1998. Magnitude of Residues in Processed Sunflower Seed. Analytical Portions of the Processing Study for Italy. Date Stamped-"Received Health Evaluation Division Mar 5 1998".(TMN-569;0292-89;0266-91;0340-91).(Clethodim)
1175025	1996. Magnitude of Clethodim Residues In Sunflowers-Seeds And Processed Parts. Date Stamped-"Received Health Evaluation Division Mar 18 1998".(V-11186;MRID#44323402) [*Note-Page#317,529,532,536 Missing]

PMRA Document Number	Reference
1184497	1998. Residue Data Submitted in Support of Minor Use of 96-522, Select to Control Annual Grasses on Dry Onions, Residue Trial Specification Form, Pesticide Residue Report from Health Canada, Method, Example Chromatograms and Laboratory Submissions Sheets and Copies of the Laboratory Reports [Select;Regn.#22625]
1196377	2005.Clethodim: Magnitude of the Residue on Fenugreek. Study No. AAFC03-049. Unpublished study prepared by Agriculture and Agri-Food Canada, Ottawa, ON. 209 pp.
1196378	2005. Clethodim: Magnitude of the Residue on Fenugreek. Final Analytical Report.
1227015	1988. The in vivo metabolism of [propyl-1-14C] clethodim in rats (2515)
1227023	1988. Plant metabolism study of [Ally-2-14C] Clethodim. Laboratory Project identification: MEF-0005, Study Volume 1 of 1; File No.: 721.14/Clethodim. Dec. 22, 1988
1227024	1988. Plant Metabolism Study of [Ring-4,6-14C]-Clethodim in Carrots, Soybeans and Cotton. TOMEN Report #149. Unpublished.
1227025	1988. Analytical Method for The Determination of Clethodim Residues (RM-26)
1227026	1988. Summary - Clethodim on Canola, Flax
1227027	1988. Select Residue Analysis 1988 Crops (Flax, Canola)
1229447	1988. The in Vivo Metabolism Of [Propyl-1-14C] Clethodim in Lactating Goat (MEF-0038)
1229468	1988. [Ring-4,6-14C] Clethodim : A Radiocarbon Metabolism Study in Laying Hens.
1229471	1989. Cow Feeding Study : Determination of Residues of Clethodim in Bovine Tissues and Milk (ADC 1124)
1229469	Clethodim (5%) and Clethodim Sulfoxide (95%) : Meat and Egg Residue Study in White Leghorn Chickens (88 EM 9), DACO: 7.5
1232663	1988. Analytical Methodology – Canola, Flax and Soybeans
1237305	1992. Confirmatory Method for the Determination of Clethodim and Clethodim Metabolites in Crops, Animal Tissues, Milk and Eggs (RM-26D-1)
1598359	2001. Clethodim: Magnitude of the Residue on Spinach. Lab Project Number: 06243.99-NYR01. Unpublished Study Prepared by IR-4 Project at Rutgers, the State University of New Jersey, North Brunswick, NJ. 261 pages.
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1701890	2008. Clethodim: Magnitude of the Residue on Blueberry. IR-4 PR No. 05234, Laboratory Identification No. 05234.04-NYR17. Unpublished study prepared by IR-4 Project Headquarters, Princeton, NJ. 265 pages. Duplicate: PMRA# 1701953
2066127	1999. Clethodim: Magnitude of Residues in/on Cranberries.14-JUN-99. (IR4 PR# 05358) Duplicate: PMRA#s 1095532, 2066155
2265024	2012. Clethodim: Magnitude of the Residue in and on Dill. Study Number AAFC03-047, Laboratory Identification Number: AAFC03-047-200. Unpublished study prepared by Pest Management Centre, Agriculture and Agri-Food Canada, Ottawa, ON, 645 pages. Duplicate: PMRA# 2265043

PMRA Document Number	Reference
2265069	2012. Clethodim: Magnitude of the Residue on Caraway. Study Number AAFC03-044, Laboratory Identification Number: AAFC03-044-200. Unpublished study prepared by Pest Management Centre, Agriculture and Agri-Food Canada, Ottawa, ON, 237 pages.
2265170	2012. AAFC04-054 Clethodim in Caraway - Final Report - Supervised Residue Trial Analytical Methodology.
2303325	2013. Aafc06-052 Centurion (Clethodim PCP#27598) Residue Report Radish - Supervised Residue Trial Analytical Methodology. Duplicate: PMRA#s 2303349, 2303370, 2303385, 2303402, 2303423
2303339	2013. Clethodim: Magnitude of the Residue on Carrot." Study No. AAFC06-053R. Laboratory Identification Number: AAFC06-053R-301. Unpublished study prepared by the Pest Management Center, Agriculture and Agri-food Canada, Ottawa, ON, 387 pages. Duplicate: PMRA#s 2303321, 2303348, 2303369, 2303384, 2303456
2348144	2013. Residue Report - Clethodim: Magnitude of the Residue on Basil – Residue Trial Analytical Methodology (Plant and/or Animal Commodities). Duplicate: PMRA# 2348190

Additional Information Considered

Foreign Reviews

PMRA Document Number	Reference
2536100	JMPR, 1994. The Joint FAO/WHO Meeting on Pesticide Residues (JMPR) JMPR Evaluation for Clethodim. JMPR no. (187)
2536103	JMPR, 1999. The Joint FAO/WHO Meeting on Pesticide Residues (JMPR) JMPR Evaluation for Clethodim. JMPR no. (187)
2536104	JMPR, 2002. The Joint FAO/WHO Meeting on Pesticide Residues (JMPR) JMPR Evaluation for Clethodim. JMPR no. (187)

E. Information Considered in the Environmental Risk Assessment

List of Studies/Information Submitted by Registrant

PMRA Document Number	Reference
1074722	2002, ACUTE TOXICITY OF CLETHODIM 240 CE TO *DAPHNIA MAGNA*. BIOAGRI LABORATORIOS LTDA. RF-0409.206.103.02. MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 90004978. GLP, UNPUBLISHED., DACO: 9.3.5
1074729	2002, ACUTE TOXICITY OF CLETHODIM 240 CE TO EARTHWORM *EISENIA FOETIDA*. BIOAGRI LABORATORIOS LTDA. RF-0409.203.109.02. MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 90005050. GLP, UNPUBLISHED., DACO: 9.2.8

1074730	2002, ACUTE TOXICITY OF CLETHODIM 240 CE TO FISH *DANIO RERIO*. BIOAGRI LABORATORIOS LTDA, RF-0409.208.098.02. MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 900004977. GLP, UNPUBLISHED., DACO: 9.5.4
1074731	2002, AVIAN ACUTE ORAL TOXICITY TEST OF CLETHODIM 240 CE IN JAPANESE QUAILS (*COTURNIX COTURNIX JAPONICA*). BIOAGRI LABORATORIOS LTDA., RF-0409.302.115.02. MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 900004975. GLP, UNPUBLISHED., DACO: 9.6.4
1074732	2002, TOXICITY OF CLETHODIM 240 CE TO ALGAE *PSEUDOKIRCHNERIELLA SUBCAPITATA*. BIOAGRI LABORATORIOS LTDA., RF-0409.202.095.02. MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 900004979. GLP, UNPUBLISHED., DACO: 9.8.6
1074744	2003, HYDROLYSIS OF CLETHODIM AGAN TECHNICAL AS FUNCTION OF PH. BIOAGRI LABORATORIOS LTDA, RF-0409.012.038.02. MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 900006023. GLP, UNPUBLISHED, DACO: 8.2.3.2
1074745	2003, PHOTOLYSIS IN WATER BY ARTIFICIAL SUNLIGHT OF CLETHODIM AGAN TECHNICAL. BIOAGRI LABORATORIOS LTDA, RF-0409.013.047.02. MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 900006022. GLP, UNPUBLISHED., DACO: 8.2.3.3.2
1074746	2003, SOIL ADSORPTION/DESORPTION OF CLETHODIM AGAN TECHNICAL. BIOAGRI LABORATORIOS LTDA, RF-0409.027.044.02. MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 900006025. GLP, UNPUBLISHED., DACO: 8.2.4.2
1074747	2002, ACUTE TOXICITY OF CLETHODIM AGAN TECHNICAL TO EARTHWORM (*EISENIA FOETIDA*). BIOAGRI LABORATORIOS LTDA, RF-0409.203.110.02. MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 900005080. GLP, UNPUBLISHED., DACO: 9.2.3.1
1074748	2002, ACUTE CONTACT TOXICITY OF CLETHODIM AGAN TECHNICAL TO HONEYBEES (*APIS MELLIFERA*) (AFRICANIZED). BIOAGRI LABORATORIOS LTDA, RF-0409.204.117.02. MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 900005081. GLP, UNPUBLISHED., DACO: 9.2.4.1
1074749	2002, ACUTE ORAL TOXICITY OF CLETHODIM AGAN TECHNICAL TO HONEYBEES (*APIS MELLIFERA*) (AFRICANIZED). BIOAGRI LABORATORIOS LTDA, RF-0409.205.015.02. MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 900005082. GLP, UNPUBLISHED., DACO: 9.2.4.2
1074750	2002, ACUTE TOXICITY OF CLETHODIM AGAN TECHNICAL TO *DAPHNIA MAGNA*. BIOAGRI LABORATORIOS LTDA, RF-0409.206.104.02. MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 900005083. GLP, UNPUBLISHED., DACO: 9.5.2
1074751	2003, ACUTE TOXICITY OF CLETHODIM AGAN TECHNICAL TO FISH *DANIO RERIO*. BIOAGRI LABORATORIOS LTDA, RF-0409.208.099.02. MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 900005085. GLP, UNPUBLISHED., DACO: 9.5.2.1
1074752	2002, AVIAN ACUTE ORAL TOXICITY OF CLETHODIM AGAN TECHNICAL IN JAPANESE QUAILS (*COTURNIX COTURNIX JAPONICA*). BIOAGRI LABORATORIOS LTDA, RF-0409.302.116.02. MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 900005089. GLP, UNPUBLISHED., DACO: 9.6.2.3

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1017454	2002, TOXICITY OF CLETHODIM AGAN TECHNICAL TO ALGAE (*PSEUDOKIRCHNERIELLA SUBCAPITATA*), BIOAGRO LABORATORIOS LTDA, RF-0409/202.096.02, MAKHTESHIM-AGAN OF NORTH AMERICA LTD., # 90909/0979, GLP, UNPUBLISHED., DACO: 9.8.2
1140/0001	1993, HERBICIDES: CLETHODIM SELECT - SOIL DISSIPATION STUDY CANADA, 1992 (93-4026 DC), DACO: 8.3.2.3
1150/0135	1993, HERBICIDES CLETHODIM SELECT SOIL DISSIPATION STUDY NOVA SCOTIA, 1992 (REF 93-4060 DC), DACO: 8.3.2.3
1226/0005	1988, HYDROLYSIS STUDY ON RE-45601 (MEF-0011/870/1099), DACO: 8.2.1
1226/0006	1988, [4,6-RING-14C] - CLETHODIM PHOTODEGRADATION IN WATER (MEF-0012/4), DACO: 8.2.1
1226/0007	1988, [ALLYL-2-14C] - CLETHODIM PHOTODEGRADATION IN WATER (MEF-0025/881150/08), DACO: 8.2.1
1226/0008	1988, CLETHODIM PHOTODEGRADATION ON SOIL (MEF-0022/880054/01), DACO: 8.2.1
1226/0009	1988, FREUNDLICH SOIL ADSORPTION/DESORPTION COEFFICIENTS OF CLETHODIM AND THREE METABOLITES (MEF-0042/882190/44), DACO: 8.2.4.1
1226/0010	1988, THE AEROBIC SOIL METABOLISM OF CLETHODIM USING [RING-4,6-14C] AND [ALLYL-2-14C] CLETHODIM (MEF-0015/0016/881957/6), DACO: 8.2.3.1
1226/0011	1988, THE AEROBIC SOIL METABOLISM OF [PROPYL-1-14C] CLETHODIM (MEF-0018&19/2/10/28), DACO: 8.2.3.1
1226/0012	1988, THE AEROBIC SOIL METHABOLSIM OF [RING-4,6-14C] CLETHODIM (MEF-0016/3/881957/8), DACO: 8.2.3.1

8227a50	[1986], ACUTE TOXICITY OF CHEVRON RE-470410 TECHNICAL TO RAINBOW TROUT (Oncorhynchus mykiss) IN A STATIC TEST SYSTEM (1486/0), DACO: 9.5.2.1
8227a60	[1988], CHARACTERIZATION OF 14C RESIDUES IN BLUEGILL SUNFISH TREATED WITH [ALLYL-2-14C]-CLETHODIM OR [CYCLOHEXENE-1-ONE-4,6-14C]-CLETHODIM, (MRID - 00156), DACO: 9.9.5
8227a61	[1987], UPTAKE, DEPURATION AND BIOCONCENTRATION OF [ALLYL-2-14C] AND [CYCLOHEXENE-1-ONE-4,6-14C] RE-470410 TO BLUEGILL SUNFISH (LEPOMIS [illegible] (MRID 00160), DACO: 9.5.3
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